					inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemorhilia, hymercoagonilation
					diabetes mellitus, endocarditis, meningitis, Lyme Disease,
					suppression of immune reactions to transplanted
					organs, asthma and allergy.
	HACBD91	954	Activation of	Assays for the activation of	A highly preferred
9			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
			response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
				(including antibodies and	blood disorders (e.g., as
				agonists or antagonists of the	described below under
				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
				modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
				assays for transcription	autoimmune diseases (e.g.,
				through the STAT6 response	rheumatoid arthritis, systemic
				element that may be used or	lupus erythematosis, multiple
				routinely modified to test	sclerosis and/or as described
				STAT6 response element	below) and
				activity of the polypeptides of	immunodeficiencies (e.g., as
				the invention (including	described below).

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Preferred indications include neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	,
antibodies and agonists or antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); Georas	et al., Blood 92(12):4529-4538	(1998); Moffatt et al.,	Transplantation 69(7):1521-	1523 (2000); Curiel et al., Eur	J Immunol 27(8):1982-1987	(1997); and Masuda et al., J	Biol Chem 275(38):29331-	29337 (2000), the contents of	each of which are herein	incorporated by reference in its	entirety. T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the SUPT cell line,	which is a suspension culture	of IL-2 and IL-4 responsive T	cells.		

reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating adipocyte highly preferred embodiment of the invention. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for simulating (e.g.,
	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and aconists or antagonists of
	Activation of Adipocyte ERK Signaling Pathway
	955
	HACCI17
	7

	the invention) include the	increasing) adipocyte
	 assavs disclosed in Forrer et	activation. An alternative
	 al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	 1110 (1998); Le Marchand-	of the invention includes a
	 Brustel Y, Exp Clin	method for inhibiting the
	 Endocrinol Diabetes	activation of (e.g., decreasing)
	 107(2):126-132 (1999);	and/or inactivating adipocytes.
	 Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	 and Karin, Nature	(e.g., as described below under
	 410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	 the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	 reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	 may be used according to these	Disorders"). Preferred
	 assays are publicly available	indications include blood
	 (e.g., through the ATCC).	disorders (e.g., hypertension,
	 Exemplary mouse adipocyte	congestive heart failure, blood
	 cells that may be used	vessel blockage, heart disease,
	 according to these assays	stroke, impotence and/or as
	include 3T3-L1 cells. 3T3-L1	described below under
	 is an adherent mouse	"Immune Activity",
	 preadipocyte cell line that is a	"Cardiovascular Disorders",
	 continuous substrain of 3T3	and/or "Blood-Related
	 fibroblast cells developed	Disorders"), immune disorders
	 through clonal isolation and	(e.g., as described below under
	undergo a pre-adipocyte to	"Immune Activity"), neural
	adipose-like conversion under	disorders (e.g., as described

below under "Neural Activity and Neurological Diseases").	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,
appropriate differentiation conditions known in the art.																													
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hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and	disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly	preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies,

					muscular dystrophy, and/or as
					described herein.
			•		Additional highly preferred
					indications include,
					hypertension, coronary artery
					disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
~					lymphoma, leukemia and
					breast, colon, and kidney
					cancer. Additional preferred
<del></del>					indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HACCI17	955	Production of IL-8	Assay that measures the	Highly preferred indications
7			by immune cells	production of the chemokine	include eosinophilia, asthma,
,			(such as the human	interleukin-8 (IL-8) from	allergy, hypersensitivity

			EOL-1 eosinophil	immune cells (such as the	reactions, inflammation, and
			cells)	EOL-1 human eosinophil cell	inflammatory disorders.
			`	line) are well known in the art	Additional highly preferred
				(for example, measurement of	indications include immune
				IL-8 production by FMAT)	and hematopoietic disorders
				and may be used or routinely	(e.g., as described below under
				modified to assess the ability	"Immune Activity", and
				of polypeptides of the	"Blood-Related Disorders"),
				invention (including antibodies	autoimmune diseases (e.g.,
				and agonists or antagonists of	rheumatoid arthritis, systemic
				the invention) to promote or	lupus erythematosis, Crohn"s
				inhibit. Eosinophils are a type	disease, multiple sclerosis
-				of immune cell important in	and/or as described below),
				allergic responses; they are	immunodeficiencies (e.g., as
				recruited to tissues and	described below). Highly
				mediate the inflammtory	preferred indications also
				response of late stage allergic	include boosting or inhibiting
				reaction. IL8 is a strong	immune cell proliferation.
				immunomodulator and may	Preferred indications include
	-			have a potential	neoplastic diseases (e.g.,
				proinflammatory role in	leukemia, lymphoma, and/or as
				immunological diseases and	described below under
				disorders (such as allergy and	"Hyperproliferative
				asthma).	Disorders"). Highly preferred
					indications include boosting an
					eosinophil-mediated immune
					response, and suppressing an
					eosinophil-mediated immune
					response.
	HACCI17	955	Activation of	This reporter assay measures	Highly preferred indications
[7			transcription	activation of the GATA-3	include allergy, asthma, and

through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
response element in	human mast cell line.	indications include infection
 immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
 as mast cells).	cells has been linked to	described below under
	cytokine and chemokine	"Infectious Disease"), and
	production. Assays for the	inflammation and
 	activation of transcription	inflammatory disorders.
	through the GATA3 response	Preferred indications also
	element are well-known in the	include blood disorders (e.g.,
	art and may be used or	as described below under
	routinely modified to assess	"Immune Activity", "Blood-
	the ability of polypeptides of	Related Disorders", and/or
	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmune diseases (e.g.,
	regulate GATA3 transcription	rheumatoid arthritis, systemic
	factors and modulate	lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	important for immune response	below) and
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
 	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred

	through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
	response element in	human mast cell line.	indications include infection
	immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
	as mast cells).	cells has been linked to	described below under
		cytokine and chemokine	"Infectious Disease"), and
		production. Assays for the	inflammation and
		activation of transcription	inflammatory disorders.
		through the Nuclear Factor of	Preferred indications also
		Activated T cells (NFAT)	include blood disorders (e.g.,
(		response element are well-	as described below under
		known in the art and may be	"Immune Activity", "Blood-
		used or routinely modified to	Related Disorders", and/or
		assess the ability of	"Cardiovascular Disorders").
		polypeptides of the invention	Preferred indications include
		(including antibodies and	autoimmune diseases (e.g.,
		agonists or antagonists of the	rheumatoid arthritis, systemic
		invention) to regulate NFAT	lupus erythematosis, multiple
		transcription factors and	sclerosis and/or as described
		modulate expression of genes	below) and
		involved in	immunodeficiencies (e.g., as
		immunomodulatory functions.	described below). Preferred
		Exemplary assays for	indications include neoplastic
		transcription through the	diseases (e.g., leukemia,
		NFAT response element that	Iymphoma, melanoma,
		may be used or routinely	prostate, breast, lung, colon,
		modified to test NFAT-	pancreatic, esophageal,
		response element activity of	stomach, brain, liver, and
		polypeptides of the invention	urinary tract cancers and/or as
		(including antibodies and	described below under
		agonists or antagonists of the	"Hyperproliferative
		invention) include assays	Disorders"). Other preferred

Gene indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.  Boer Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.  Iline heral st
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disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., I Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of

		HACCI17	955	Production of IL-5	IL-5 FMAT. Assays for	A highly preferred
	7				immunomodulatory proteins	embodiment of the invention
					secreted by TH2 cells, mast	includes a method for
· -					cells, basophils, and	inhibiting (e.g., reducing) IL-5
					eosinophils that stimulate	production. An alternative
					eosinophil function and B cell	highly preferred embodiment
					Ig production and promote	of the invention includes a
					polarization of CD4+ cells into	method for stimulating (e.g.,
					TH2 cells are well known in	increasing) IL-5 production.
					the art and may be used or	A highly preferred
					routinely modified to assess	embodiment of the invention
					the ability of polypeptides of	includes a method for
		-			the invention (including	stimulating (e.g., increasing)
					antibodies and agonists or	immunoglobulin production.
					antagonists of the invention) to	An alternative highly preferred
51					mediate immunomodulation,	embodiment of the invention
3					stimulate immune cell	includes a method for
					function, modulate B cell Ig	inhibiting (e.g., decreasing)
					production, modulate immune	immunoglobulin production.
					cell polarization, and/or	A highly preferred indication
					mediate humoral or cell-	includes allergy. A highly
					mediated immunity.	preferred indication includes
					Exemplary assays that test for	asthma. A highly preferred
					immunomodulatory proteins	indication includes rhinitis.
					evaluate the production of	An additional highly preferred
					cytokines, such as IL-5, and	indication is infection (e.g., an
					the stimulation of eosinophil	infectious disease as described
					function and B cell Ig	below under "Infectious
					production. Such assays that	Disease"), and inflammation
		——————————————————————————————————————			may be used or routinely	and inflammatory disorders.
					modified to test	Preferred indications include

				cells mediate humoral or cell-	Preferred indications include
				mediated immunity and may	anemia, pancytopenia,
				be preactivated to enhance	leukopenia, thrombocytopenia,
				responsiveness to	leukemias, Hodgkin's disease,
				immunomodulatory factors.	acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					immune reactions to
					transplanted organs and
					tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, and Lyme Disease.
	HACCI17	955	Production of	Endothelial cells, which are	Highly preferred indications
7			ICAM in	cells that line blood vessels,	include inflammation (acute
			endothelial cells	and are involved in functions	and chronic), restnosis,
			(such as human	that include, but are not limited	atherosclerosis, asthma and
			umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
			endothelial cells	permeability, vascular tone,	indications include
			(HUVEC))	and immune cell extravasation.	inflammation and
				Exemplary endothelial cells	inflammatory disorders,
				that may be used in ICAM	immunological disorders,
				production assays include	neoplastic disorders (e.g.
				human umbilical vein	cancer/tumorigenesis), and
				endothelial cells (HUVEC),	cardiovascular disorders (such
				and are available from	as described below under

		commercial sources The	"Immine Activity" "Blood-
		expression of ICAM (CD54),a	Related Disorders",
 		intergral membrane protein,	"Hyperproliferative Disorders"
		can be upregulated by	and/or "Cardiovascular
 		cytokines or other factors, and	Disorders"). Highly preferred
 -		ICAM expression is important	indications include neoplasms
		in mediating immune and	and cancers such as, for
		endothelial cell interactions	example, leukemia, lymphoma,
<u></u>		leading to immune and	melanoma, renal cell
		inflammatory responses.	carcinoma, and prostate,
 		Assays for measuring	breast, lung, colon, pancreatic,
		expression of ICAM-1 are	esophageal, stomach, brain,
 		well-known in the art and may	liver and urinary cancer. Other
 		be used or routinely modified	preferred indications include
 		to assess the ability of	benign dysproliferative
 		polypeptides of the invention	disorders and pre-neoplastic
		(including antibodies and	conditions, such as, for
		agonists or antagonists of the	example, hyperplasia,
		invention) to regulate ICAM-1	metaplasia, and/or dysplasia.
		expression. Exemplary assays	
		that may be used or routinely	
 		modified to measure ICAM-1	
 ~		expression include assays	
		disclosed in: Rolfe BE, et al.,	
 		Atherosclerosis, 149(1):99-110	
 		(2000); Panettieri RA Jr, et al.,	
 		J Immunol, 154(5):2358-2365	
 		(1995); and, Grunstein MM, et	
	-	al., Am J Physiol Lung Cell	
		Mol Physiol, 278(6):L1154-	
 		L1163 (2000), the contents of	

				each of which is herein	
				incorporated by reference in its	
				entirety.	
	HACCI17	955	Production of IL-8	Assays measuring production	Highly preferred indications
7			by by endothelial	of IL-8 are well known in the	include immunological and
			cells (such as	art and may be used or	inflammatory disorders (e.g.,
			Human Umbilical	routinely modified to assess	such as allergy, asthma,
			Cord Endothelial	the ability of polypeptides of	leukemia, etc. and as described
			Cells).	the invention (including	below under "Immune
				antibodies and agonists or	Activity", and "Blood-Related
				antagonists of the invention) to	Disorders"). Highly preferred
				regulate production and/or	indications also includie
			-	secretion of IL-8. For	autoimmune disorders (e.g.,
				example, FMAT may be used	rheumatoid arthritis, systemic
				or routinely modified to assess	lupus erythematosis, Crohn"s
				the ability of polypeptides of	disease, multiple sclerosis
				the invention (including	and/or as described below),
				antibodies and agonists or	neoplastic disorders (e.g.,
				antagonists of the invention) to	organ cancers such as lung,
				regulate production and/or	liver, colon cancer, and/or as
				secretion of IL-8 from	described below under
				endothelial cells (such as	"Hyperproliferative
				human umbilical vein	Disorders"), and
				endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
				HUVECs are endothelial cells	such as described below under
				which line venous blood	"Cardiovascular Disorders").
				vessels, and are involved in	Preferred indications include
				functions that include, but are	thrombosis, bacteremia and
				not limited to, angiogenesis,	sepsis syndrome and
				vascular permeability, vascular	consequent complications
				tone, and immune cell	(such as acute respiratory

 HACC117	955	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	extravasation. Endothelial cells play a pivotal role in the initiation and perpetuation of IL-8 may play an important role in recruitment and activation of immune cells such as neutrophils, macrophages, and lymphocytes.  RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or	distress syndrome and systemic ischemia-reperfusion resulting from septic shock), restnosis and atherosclerosis.
			mediate humoral or cell- mediated immunity.  Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in	

immune cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407	which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are

			involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	
HACCI17	955	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC),	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred inflammation and inflammation and inflammatory disorders, immunological disorders, earcer/tumorigenesis), and cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred indications include neoplasms and cancers such as, for example, leukemia, lymphoma, melanoma, renal cell carcinoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,
	HACCI17		955	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))

				commercial sources. The expression of VCAM (CD106), a membraneassociated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
∞	HADA089	956	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described

below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	arthritis, asthma, AIDS,	allergy, anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),
agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1988); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Rellahan et al., J Biol Chem	272(49):30806-30811 (1997);	Chang et al., Mol Cell Biol	18(9):4986-4993 (1998); and	Fraser et al., Eur J Immunol	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Mouse T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the HT2 cell	line, which is an IL-2	dependent suspension culture	cell line that also responds to	IL-4.			
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plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	
	expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes-macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine. Assays for immunomodulatory proteins that promote the production of GM-CSF are well known in the art and may be used or routinely modified
	Production of GM-CSF
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under "Immune Activity", "Blood-Related Disorders"	blood-neigled Disolders,	allu/oi Caluiovasculai	Disorders   Highly preferred   indications of a line line line line line line line line	mulcauons also include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include asthma. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia (e.g., acute	lymphoblastic leukemia, and	acute myelogenous leukemia),	lymphoma (e.g., non-	Hodgkin"s lymphoma and	Hodgkin's disease), and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach brain liver and
to assess the ability of	(polypepudes of the invention)	(including annibonies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	modulate the growth and	differentiation of leukocytes.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as GM-CSF,	and the activation of T cells.	Such assays that may be used	or routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Ye et al., J Leukoc	Biol (58(2):225-233, the	contents of each of which are	herein incorporated by	reference in its entirety.	Natural killer cells that may be
											,		-										-				_			

urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications		response, and alternatively, suppressing a T cell-mediated immune response. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,
used according to these assays are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large	granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cellmediated cytotoxicity.	

					meningitis, Lyme Disease, and allergy.
	HAGAI85	957	Production of	IFNgamma FMAT. IFNg	A highly preferred
6			IFNgamma using	plays a central role in the	embodiment of the invention
			Natural Killer cells	immune system and is	includes a method for
				considered to be a	stimulating the production of
				proinflammatory cytokine.	IFNg. An alternative highly
				IFNg promotes TH1 and	preferred embodiment of the
				inhibits TH2; promotes IgG2a	invention includes a method
				and inhibits IgE; induces	for inhibiting the production of
				macrophage activation; and	IFNg. Highly preferred
				increases MHC expression.	indications include blood
				Assays for immunomodulatory	disorders (e.g., as described
				proteins produced by T cells	below under "Immune
				and NK cells that regulate a	Activity", "Blood-Related
				variety of inflammatory	Disorders",
				activities and inhibit TH2	"Hyperproliferative Disorders"
				helper cell functions are well	(e.g. cancer/tumorigenesis)
				known in the art and may be	and/or "Cardiovascular
				used or routinely modified to	Disorders"), and infection
				assess the ability of	(e.g., viral infections,
		·		polypeptides of the invention	tuberculosis, infections
				(including antibodies and	associated with chronic
				agonists or antagonists of the	granulomatosus disease and
				invention) to mediate	malignant osteoporosis, and/or
				immunomodulation, regulate	as described below under
				inflammatory activities,	"Infectious Disease"). Highly
				modulate TH2 helper cell	preferred indications include
				function, and/or mediate	autoimmune disease (e.g.,
				humoral or cell-mediated	rheumatoid arthritis, systemic
				immunity. Exemplary assays	lupus erythematosis, multiple

sclerosis and/or as described below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response, boosting	antibody-dependent immune	responses, suppressing	antibody-dependent immune	responses, boosting innate	immunity and immune	responses, and suppressing	innate immunity and immune	responses. Additional highly	preferred indications include	inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	may be used according to these example, leukemia, lymphoma,
that test for immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad	Sci 856:22-32 (1998); Boehm	et al., Annu Rev Immunol	15:749-795 (1997), and	Rheumatology (Oxford)	38(3):214-20 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Natural Killer (NK) cells that	may be used according to these
						·	~							•															-
								-																					

				assays are publicly available	melanoma, and prostate,
				(e.g., through the AICC) or	breast, lung, colon, pancreatic,
				may be isolated using	esophageal, stomach, brain,
				techniques disclosed herein or	liver and urinary cancer. Other
				otherwise known in the art.	preferred indications include
				Natural killer (NK) cells are	benign dysproliferative
				large granular lymphocytes	disorders and pre-neoplastic
				that have cytotoxic activity but	conditions, such as, for
				do bind antigen. NK cells	example, hyperplasia,
				show antibody-independent	metaplasia, and/or dysplasia.
				killing of tumor cells and also	Preferred indications include
				recognize antibody bound on	anemia, pancytopenia,
				target cells, via NK Fc	leukopenia, thrombocytopenia,
				receptors, leading to cell-	Hodgkin's disease, acute
				mediated cytotoxicity.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
		         			asthma and allergy.
	HAGAM64	856	Regulation of	Caspase Apoptosis. Assays for Preferred embodiments of the	Preferred embodiments of the
10			apoptosis of	caspase apoptosis are well	invention include using
			immune cells (such	known in the art and may be	polypeptides of the invention

as mast cells).	used or routinely modified to	for antibodies, agonists, or
	assess the ability of	antagonists thereof) in
,	polypeptides of the invention	detection, diagnosis,
	(including antibodies and	prevention, and/or treatment of
	agonists or antagonists of the	asthma, allergy,
	invention) to regulate caspase	hypersensitivity and
	protease-mediated apoptosis in	inflammation.
	immune cells (such as, for	
	example, in mast cells). Mast	
 -	cells are found in connective	
	and mucosal tissues throughout	
 	the body, and their activation	
	via immunoglobulin E -	
 	antigen, promoted by T helper	
	cell type 2 cytokines, is an	
	important component of	
	allergic disease. Dysregulation	
	of mast cell apoptosis may	
	play a role in allergic disease	
	and mast cell tumor survival.	
	Exemplary assays for caspase	
	apoptosis that may be used or	
	routinely modified to test	
	capase apoptosis activity	
	induced by polypeptides of the	
	invention (including antibodies	
	and agonists or antagonists of	
	the invention) include the	
	assays disclosed in: Masuda A,	
	et al., J Biol Chem,	
	276(28):26107-26113 (2001);	

Lett 0); Nor 209- and hromb ch are ch are se used //s are Irces). Is that to these is such st cell	Highly preferred indications include neoplastic diseases ivation (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma iists of (e.g., T cell lymphoma, non-
Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Assays for the activation of transcription through the Gamma Interferon Activation at in Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate
	Activation of transcription through GAS response element in immune cells (such as T-cells).
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	HAG 11

STAT transcription factors and
modulate gene expression
involved in a wide variety of
cell functions. Exemplary
assays for transcription
through the GAS response
element that may be used or
routinely modified to test
GAS-response element activity
of polypeptides of the
invention (including antibodies
and agonists or antagonists of
the invention) include assays
disclosed in Berger et al., Gene
66:1-10 (1998); Cullen and
Malm, Methods in Enzymol
216:362-368 (1992); Henthorn
et al., Proc Natl Acad Sci USA
85:6342-6346 (1988);
Matikainen et al., Blood
93(6):1980-1991 (1999); and
Henttinen et al., J Immunol
155(10):4582-4587 (1995), the
contents of each of which are
herein incorporated by
reference in its entirety.
Exemplary mouse T cells that
may be used according to these
assays are publicly available
(e.g., through the ATCC).
Exemplary T cells that may be

				used according to these assays include the CTLL cell line, which is a suspension culture	"Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis,
				of IL-2 dependent cytotoxic T cells.	infections associated with chronic granulomatosus disease and malignant
					osteoporosis, and/or an infectious disease as described below under "Infectious
					Disease"). An additional preferred indication is idionathic nulmonary fibrosis
					Preferred indications include anemia, pancytopenia,
					leukopenia, thrombocytopenia, acute lymphocytic anemia
					(ALL), plasmacytomas, multiple myeloma, arthritis,
					AIDS, granulomatous disease, inflammatory bowel disease,
					sepsis, neutropenia, neutrophilia, psoriasis,
					suppression of immune reactions to transplanted
					organs and tissues,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and asthma and alleroy.
12	HAGBZ81	096	Activation of transcription	Assays for the activation of transcription through the	A preferred embodiment of the invention includes a

		through serum	Serum Kesponse Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate the serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth. Exemplary assays	Activity", "Blood-Related
			for transcription through the	Disorders", and/or
			SRE that may be used or	"Cardiovascular Disorders"),
			routinely modified to test SRE	Highly preferred indications
			activity of the polypeptides of	include autoimmune diseases
13			the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
			antagonists of the invention)	Crohn"s disease, multiple
			include assays disclosed in	sclerosis and/or as described
	<b>1</b> 0		Berger et al., Gene 66:1-10	below), immunodeficiencies
			(1998); Cullen and Malm,	(e.g., as described below),
			Methods in Enzymol 216:362-	boosting a T cell-mediated
			368 (1992); Henthorn et al.,	immune response, and
			Proc Natl Acad Sci USA	suppressing a T cell-mediated
			85:6342-6346 (1988); and	immune response. Additional
			Black et al., Virus Genes	highly preferred indications
			12(2):105-117 (1997), the	include inflammation and
		-	content of each of which are	inflammatory disorders, and
			herein incorporated by	treating joint damage in
			reference in its entirety. T	patients with rheumatoid

						<del></del>
arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases		highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,	melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.  Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,
cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2	dependent suspension culture of T cells with cytotoxic activity.				
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arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular
	Inhibition of squalene synthetase gene transcription.
	961
	HAGDG59
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carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for the activation of transcription through the well-known in the art and may inflammation. Preferred indications described below under antagonists of the invention) to regulate NFKB inflammation and inflammatory disorders, invention) to regulate NFKB inflammation and inflammatory disorders, inflammatory disorders, inflammatory disorders (e.g., an antagonists of the invention) include assays disclosed in Berger et al., Gene
carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	such
	transcription through NFKB response eleme immune cells (s as EOL1 cells).
	HAGDI35
	14

Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle Blazquez et al, Immunology	90(3):455-460 (1997); Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3).030-044 (1999), the contents of each of	which are herein incorporated	by reference in its entirety.	For example, a reporter assay	(which measures increases in	transcription inducible from a	NFkB responsive element in	EOL-1 cells) may link the	NFKB element to a repeorter	gene and binds to the NFKB	transcription factor, which is	upregulated by cytokines and	other factors. Exemplary	immune cells that may be used	according to these assays	include eosinophils such as the	human EOL-1 cell line of	eosinophils. Eosinophils are a	type of immune cell important	in the allergic responses; they	are recruited to tissues and	mediate the inflammtory

				response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.	
	HAGDI35	962	Activation of	This reporter assay measures	Highly preferred indications
14			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
			-	element are well-known in the	include blood disorders (e.g.,
			-	art and may be used or	as described below under
		170		routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
	- 14			antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,
				routinely modified to test	lymphoma, melanoma,
				GATA3-response element	prostate, breast, lung, colon,
				activity of polypeptides of the	pancreatic, esophageal,

stomach, brain, liver, and urinary tract cancers and/or as described below under "Hyperproliferative "Picadom" (14)	Disorders ). Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia	(ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease,	inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,	meningius, and Lyme Disease.
invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Podriguez Polymero et al. Eur.	J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by	reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g.,	Exemplary human mast cells that may be used according to these assays include the HMC-	immature human mast cell line established from the peripheral blood of a patient with mast

				cell leukemia, and exhibits	
-				many characteristics of	
				immature mast cells.	
	HAGDI35	296	Production of	Endothelial cells, which are	Highly preferred indications
14			ICAM in	cells that line blood vessels,	include inflammation (acute
			endothelial cells	and are involved in functions	and chronic), restnosis,
			such as human	that include, but are not limited	atherosclerosis, asthma and
			umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
			endothelial cells	permeability, vascular tone,	indications include
			(HUVEC))	and immune cell extravasation.	inflammation and
				Exemplary endothelial cells	inflammatory disorders,
				that may be used in ICAM	immunological disorders,
				production assays include	neoplastic disorders (e.g.
-				human umbilical vein	cancer/tumorigenesis), and
		_		endothelial cells (HUVEC),	cardiovascular disorders (such
				and are available from	as described below under
				commercial sources. The	"Immune Activity", "Blood-
				expression of ICAM (CD54),a	Related Disorders",
				intergral membrane protein,	"Hyperproliferative Disorders"
				can be upregulated by	and/or "Cardiovascular
				cytokines or other factors, and	Disorders"). Highly preferred
				ICAM expression is important	indications include neoplasms
				in mediating immune and	and cancers such as, for
				endothelial cell interactions	example, leukemia, lymphoma,
				leading to immune and	melanoma, renal cell
				inflammatory responses.	carcinoma, and prostate,
				Assays for measuring	breast, lung, colon, pancreatic,
				expression of ICAM-1 are	esophageal, stomach, brain,
-				well-known in the art and may	liver and urinary cancer. Other
		,		be used or routinely modified	preferred indications include
				to assess the ability of	benign dysproliferative

				polypeptides of the invention	disorders and pre-neoplastic
				(including antibodies and	conditions, such as, for
				agonists or antagonists of the	example, hyperplasia,
				invention) to regulate ICAM-1	metaplasia, and/or dysplasia.
				expression. Exemplary assays	
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Rolfe BE, et al.,	
				Atherosclerosis, 149(1):99-110	
				(2000); Panettieri RA Jr, et al.,	
				J Immunol, 154(5):2358-2365	
				(1995); and, Grunstein MM, et	
				al., Am J Physiol Lung Cell	
				Mol Physiol, 278(6):L1154-	
				L1163 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
		!		entirety.	
i	HAGDI35	796	Production of IL-8	Assays measuring production	Highly preferred indications
14			by by endothelial	of IL-8 are well known in the	include immunological and
			cells (such as	art and may be used or	inflammatory disorders (e.g.,
			Human Umbilical	routinely modified to assess	such as allergy, asthma,
			Cord Endothelial	the ability of polypeptides of	leukemia, etc. and as described
			Cells).	the invention (including	below under "Immune
				antibodies and agonists or	Activity", and "Blood-Related
				antagonists of the invention) to	Disorders"). Highly preferred
				regulate production and/or	indications also includie
		=		secretion of IL-8. For	autoimmune disorders (e.g.,
-				example, FMAT may be used	rheumatoid arthritis, systemic
				or routinely modified to assess	lupus erythematosis, Crohn"s

				the ability of polypeptides of	disease, multiple sclerosis
				the invention (including	and/or as described below),
				antibodies and agonists or	neoplastic disorders (e.g.,
				antagonists of the invention) to	organ cancers such as lung,
				regulate production and/or	liver, colon cancer, and/or as
				secretion of IL-8 from	described below under
				endothelial cells (such as	"Hyperproliferative
			~	human umbilical vein	Disorders"), and
				endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
				HUVECs are endothelial cells	such as described below under
				which line venous blood	"Cardiovascular Disorders").
				vessels, and are involved in	Preferred indications include
				functions that include, but are	thrombosis, bacteremia and
				not limited to, angiogenesis,	sepsis syndrome and
				vascular permeability, vascular	consequent complications
				tone, and immune cell	(such as acute respiratory
				extravasation. Endothelial	distress syndrome and
-				cells play a pivotal role in the	systemic ischemia-reperfusion
				initiation and perpetuation of	resulting from septic shock),
				inflammation and secretion of	restnosis and atherosclerosis.
				IL-8 may play an important	
				role in recruitment and	
				activation of immune cells	
				such as neutrophils,	
				macrophages, and	
				lymphocytes.	
   	HAGDI35	296	Production of	Assays for measuring	Highly preferred indications
14			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
**			such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred

	endothelial cells	polypeptides of the invention	indications include
	(HUVEC))	(including antibodies and	inflammation and
	·	agonists or antagonists of the	inflammatory disorders,
-		invention) to regulate VCAM	immunological disorders,
		expression. For example,	neoplastic disorders (e.g.
		FMAT may be used to meaure	cancer/tumorigenesis), and
		the upregulation of cell surface	cardiovascular disorders (such
		VCAM-1 expresssion in	as described below under
		endothelial cells. Endothelial	"Immune Activity", "Blood-
		cells are cells that line blood	Related Disorders",
		vessels, and are involved in	"Hyperproliferative Disorders"
		functions that include, but are	and/or "Cardiovascular
		not limited to, angiogenesis,	Disorders"). Highly preferred
		vascular permeability, vascular	indications include neoplasms
		tone, and immune cell	and cancers such as, for
		extravasation. Exemplary	example, leukemia, lymphoma,
	-	endothelial cells that may be	melanoma, renal cell
		used according to these assays	carcinoma, and prostate,
		include human umbilical vein	breast, lung, colon, pancreatic,
		endothelial cells (HUVEC),	esophageal, stomach, brain,
		which are available from	liver and urinary cancer. Other
		commercial sources. The	preferred indications include
		expression of VCAM	benign dysproliferative
		(CD106), a membrane-	disorders and pre-neoplastic
		associated protein, can be	conditions, such as, for
		upregulated by cytokines or	example, hyperplasia,
		other factors, and contributes	metaplasia, and/or dysplasia.
		to the extravasation of	
	-	lymphocytes, leucocytes and	
		other immune cells from blood	
		vessels; thus VCAM	

				expression plays a role in	
				promoting immune and	
	HAGDI35	962	Activation of	This reporter assay measures	Highly preferred indication
14		,	transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
			response element in	human basophil cell line.	preferred indications include
			immune cells (such	Assays for the activation of	infection (e.g., an infectious
			as basophils).	transcription through the	disease as described below
				NFKB response element are	under "Infectious Disease"),
				well-known in the art and may	and inflammation and
				be used or routinely modified	inflammatory disorders.
				to assess the ability of	Preferred indications include
				polypeptides of the invention	immunological and
				(including antibodies and	hempatopoietic disorders (e.g.,
				agonists or antagonists of the	as described below under
				invention) to regulate NFKB	"Immune Activity", and
				transcription factors and	"Blood-Related Disorders").
		_		modulate expression of	Preferred indications also
-				immunomodulatory genes.	include autoimmune diseases
				Exemplary assays for	(e.g., rheumatoid arthritis,
				transcription through the	systemic lupus erythematosis,
				NFKB response element that	multiple sclerosis and/or as
				may be used or rountinely	described below) and
				modified to test NFKB-	immunodeficiencies (e.g., as
		-		response element activity of	described below). Preferred
				polypeptides of the invention	indications also include
				(including antibodies and	neoplastic diseases (e.g.,
				agonists or antagonists of the	leukemia, lymphoma,
				invention) include assays	melanoma, and/or as described
				disclosed in Berger et al., Gene	below under

"Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, urinary tract cancers and as described below under "Hyperproliferative Disorders".	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method
66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Marone et al, Int Arch Allergy Immunol 114(3):207-17 (1997), the contents of each of which are herein incorporated by reference in its entirety. Basophils that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of
	Activation of transcription through serum response element in immune cells (such as T-cells).
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for stimulating (e.g., increasing) TNF alpha production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,
the invention (including antibodies and agonists or antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that
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slow ttive nally, ations	xample, g., olid breast,	c, brain, er. Other include	ve plastic or	splasia. include	t, cytopenia, cute (ALL),	iple ymphoma, ılomatous y bowel	s, ne
and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel	disease, neutropenia, neutrophilia, psoriasis, suppression of immune
and/or as under "F Disorder highly p	cancers, leukemis melanon malignar tumors,	lung, co esophag liver and preferre	benign c disorder conditio	example metapla Preferre	anemia, leukope Hodgkii lympho	plasmac myelom arthritis disease,	disease, neutrop suppres
may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic	activity.						
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reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation.  A highly preferred embodiment of the invention includes a method
	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies
	Activation of Adipocyte ERK Signaling Pathway
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for stimulating (e.g., increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural
and agonists or antagonists of the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to
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disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under "Infectious Disease").  A hiohly preferred indication	is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephronathy and/or other	diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, importance (e.g., due to diabetic	neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis,
adipose-like conversion under appropriate differentiation conditions known in the art.			

microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems
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					including myopainies,
					muscular dystrophy, and/or as
					described herein.
					Additional highly preferred
					indications include,
					hypertension, coronary artery
					disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
		~			and kidney diseases or
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
					lymphoma, leukemia and
5.5					breast, colon, and kidney
					cancer. Additional preferred
					indications include melanoma,
	-				prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
		,			liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HAGFY16	965	Activation of	This reporter assay measures	Highly preferred indications
17			transcription	activation of the GATA-3	include allergy, asthma, and

	through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
	response element in	human mast cell line.	indications include infection
	immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
	as mast cells).	cells has been linked to	described below under
	`	cytokine and chemokine	"Infectious Disease"), and
	-	production. Assays for the	inflammation and
		activation of transcription	inflammatory disorders.
		through the GATA3 response	Preferred indications also
		element are well-known in the	include blood disorders (e.g.,
		art and may be used or	as described below under
		routinely modified to assess	"Immune Activity", "Blood-
		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
	N 1.	through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
,		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred

				Malm Methods in Enzymol	indications include benign
		•		216:362-368 (1992): Henthorn	dysproliferative disorders and
				et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
				85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	•			J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
-				cell leukemia, and exhibits	
-			-	many characteristics of	
				immature mast cells.	
18	HAHDB16	996	Activation of Adinocyte FRK	Kinase assay. Kinase assays, for example an Elk-1 kinase	A highly preferred embodiment of the invention
10			Training of and inter-		

Signaling Pathway	assay, for ERK signal	includes a method for
	transduction that regulate cell	stimulating adipocyte
	proliferation or differentiation	proliferation. An alternative
	are well known in the art and	highly preferred embodiment
	may be used or routinely	of the invention includes a
	modified to assess the ability	method for inhibiting
 	of polypeptides of the	adipocyte proliferation. A
	invention (including antibodies	highly preferred embodiment
	and agonists or antagonists of	of the invention includes a
4.0	the invention) to promote or	method for stimulating
	inhibit cell proliferation,	adipocyte differentiation. An
 -	activation, and differentiation.	alternative highly preferred
	Exemplary assays for ERK	embodiment of the invention
	kinase activity that may be	includes a method for
 	used or routinely modified to	inhibiting adipocyte
	test ERK kinase-induced	differentiation. A highly
	activity of polypeptides of the	preferred embodiment of the
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications

	Biol 71(3-4):479-500 (1999):	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
 	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	according to these assays	stroke, impotence and/or as
	include 3T3-L1 cells. 3T3-L1	described below under
	is an adherent mouse	"Immune Activity",
	preadipocyte cell line that is a	"Cardiovascular Disorders",
	continuous substrain of 3T3	and/or "Blood-Related
	fibroblast cells developed	Disorders"), immune disorders
	through clonal isolation and	(e.g., as described below under
	undergo a pre-adipocyte to	"Immune Activity"), neural
	adipose-like conversion under	disorders (e.g., as described
	appropriate differentiation	below under "Neural Activity
	conditions known in the art.	and Neurological Diseases"),
		and infection (e.g., as
		described below under
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
		additional highly preferred
		indication is a complication
 		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease

	(e.g., renal failure,	ıl failure,
	nephropa	nephropathy and/or other
	diseases a	diseases and disorders as
	described	described in the "Renal
	Disorders	Disorders" section below),
	diabetic n	diabetic neuropathy, nerve
	disease ar	disease and nerve damage
	(e.g., due	(e.g., due to diabetic
	neuropat	neuropathy), blood vessel
	blockage,	blockage, heart disease, stroke,
	 impotence	impotence (e.g., due to diabetic
	neuropath	neuropathy or blood vessel
	blockage	blockage), seizures, mental
	confusion	confusion, drowsiness,
	nonketoti	nonketotic hyperglycemic-
	hyperosm	hyperosmolar coma,
	cardiovas	cardiovascular disease (e.g.,
	heart dise	heart disease, atherosclerosis,
	microvas	microvascular disease,
	 hypertens	hypertension, stroke, and other
	diseases	diseases and disorders as
	described in the	in the
	"Cardiova	"Cardiovascular Disorders"
	section be	section below), dyslipidemia,
	 endocrine	endocrine disorders (as
	 described	described in the "Endocrine
-	Disorders	Disorders" section below),
	neuropat	neuropathy, vision impairment
	(e.g., dial	(e.g., diabetic retinopathy and
	 blindness	blindness), ulcers and impaired
	wound he	wound healing, infection (e.g.,

infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the	urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with	obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are	complications associated with insulin resistance. Additional highly preferred indications are disorders of the managing developed.	including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include,	hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neonlasms

and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Activation of Assays for the activation of transcription transcription through the transcription t
	HAHDB16 966 Activative transcrip transcrip through cresponse (CRE) ir adipocyt

	3T3-I	3T3-L1/CRE reporter assay may be used to identify factors	diseases and disorders as described in the "Renal
	that a	that activate the cAMP	Disorders" section below),
	signal	signaling pathway. CREB	diabetic neuropathy, nerve
	plays	plays a major role in	disease and nerve damage
	adipo	adipogenesis, and is involved	(e.g., due to diabetic
	in dif	in differentiation into	neuropathy), blood vessel
	adipo	adipocytes. CRE contains the	blockage, heart disease, stroke,
	bindi	binding sequence for the	impotence (e.g., due to diabetic
	transc	transcription factor CREB	neuropathy or blood vessel
	CRE	(CRE binding protein).	blockage), seizures, mental
	Exem	Exemplary assays for	confusion, drowsiness,
	transc	transcription through the	nonketotic hyperglycemic-
	cAMI	cAMP response element that	hyperosmolar coma,
	may l	may be used or routinely	cardiovascular disease (e.g.,
	ipou	modified to test cAMP-	heart disease, atherosclerosis,
	respo	response element activity of	microvascular disease,
	polyp	polypeptides of the invention	hypertension, stroke, and other
	(inclu	(including antibodies and	diseases and disorders as
,	agoni	agonists or antagonists of the	described in the
	inven	invention) include assays	"Cardiovascular Disorders"
	discle	disclosed in Berger et al., Gene	section below), dyslipidemia,
	66:1-	66:1-10 (1998); Cullen and	endocrine disorders (as
	Malm	Malm, Methods in Enzymol	described in the "Endocrine
	216:3	216:362-368 (1992); Henthorn	Disorders" section below),
	et al.,	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	85:63	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	et al.,	et al., Mol Cell Biol	blindness), ulcers and impaired
	20(3)	20(3):1008-1020 (2000); and	wound healing, and infection
	Klem	Klemm et al., J Biol Chem	(e.g., infectious diseases and
	273:9	273:917-923 (1998), the	disorders as described in the

				contents of each of which are	"Infectious Diseases" section below esnecially of the
				reference in its entirety. Pre-	urinary tract and skin), carpal
			- 1	adipocytes that may be used	tunnel syndrome and
				according to these assays are	Dupuytren's contracture).
				publicly available (e.g.,	Additional highly preferred
				through the ATCC) and/or	indications are complications
				may be routinely generated.	associated with insulin
-				Exemplary mouse adipocyte	resistance.
				cells that may be used	
		-		according to these assays	
				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
•				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	-
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
	HAHDB16	996	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
18			IFNgamma using a	a central role in the immune	embodiment of the invention
			T cells	system and is considered to be	includes a method for
				a proinflammatory cytokine.	stimulating the production of
				IFNg promotes TH1 and	IFNg. An alternative highly
				inhibits TH2 differentiation;	preferred embodiment of the
				promotes IgG2a and inhibits	invention includes a method
				IgE secretion; induces	for inhibiting the production of
				macrophage activation; and	IFNg. Highly preferred
	1			increases MHC expression.	indications include blood

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disorders (e.g., as described below under "Immune	Activity', Blood-Kelated Disorders', and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include
Assays for immunomodulatory proteins produced by T cells	and INK cells that regulate a variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the
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neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative	Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,	melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include benion dysproliferative	disorders and pre-neoplastic conditions, such as, for	example, nyperplasta, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease inflammatory bowel	disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune
invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical	approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad	Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and	Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are	herein incorporated by reference in its entirety.	ruman 1 cells that may be used according to these assays may be isolated using techniques disclosed herein or	otherwise known in the art. Human T cells are primary human lymphocytes that	express a T Cell receptor and CD3, CD4, or CD8. These	mediated immunity and may be preactivated to enhance responsiveness to

				immunomodulatory factors.	reactions to transplanted
				•	To the second se
					organis and dissues,
			_		nemopinia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
ì					asthma and allergy.
	HAHDR32	296	Inhibition of	Reporter Assay: construct	
19			squalene synthetase	contains regulatory and coding	
			gene transcription.	sequence of squalene	
				synthetase, the first specific	,
				enzyme in the cholesterol	
				biosynthetic pathway. See	
				Jiang, et al., J. Biol. Chem.	
				268:12818-128241(993), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety Cells were treated	
				with OTD and and and	
				with SID supernatants, and	
				SEAP activity was measured	
				after 72 hours. HepG2 is a	
				human hepatocellular	
				carcinoma cell line (ATCC	
				HB-8065). See Knowles et al.,	
				Science. 209:497-9 (1980), the	
				contents of which are herein	
				incorporated by reference in its	
	 			entirety.	
	HAHDR32	296	Activation of	Assays for the activation of	Highly preferred indications
19			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
		t			

	immune cells (such	be used or routinely modified	include blood disorders (e.g.,
	as T-cells).	to assess the ability of	as described below under
		polypeptides of the invention	"Immune Activity", "Blood-
		(including antibodies and	Related Disorders", and/or
		agonists or antagonists of the	"Cardiovascular Disorders").
		invention) to regulate NFKB	Highly preferred indications
		transcription factors and	include autoimmune diseases
-		modulate expression of	(e.g., rheumatoid arthritis,
		immunomodulatory genes.	systemic lupus erythematosis,
		Exemplary assays for	multiple sclerosis and/or as
		transcription through the	described below), and
		NFKB response element that	immunodeficiencies (e.g., as
		may be used or rountinely	described below). An
		modified to test NFKB-	additional highly preferred
		response element activity of	indication is infection (e.g.,
		polypeptides of the invention	AIDS, and/or an infectious
		(including antibodies and	disease as described below
		agonists or antagonists of the	under "Infectious Disease").
		invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	-	al., Virus Gnes 15(2):105-117	indications include neoplasms
		(1997); and Fraser et al.,	and cancers, such as, for
		29(3):838-844 (1999), the	example, melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,
		herein incorporated by	lymphoma, and prostate,
		reference in its entirety.	breast, lung, colon, pancreatic,

			Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative
		-	(e.g., through the ATCC).	disorders and pre-neoplastic conditions, such as, for
		-		example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also
				include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodokin's disease, acute
				lymphocytic anemia (ALL), plasmacytomas, multiple
				myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous
				disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis.
				hemophilia, hypercoagulation, diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, suppression of immune reactions to transplanted
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0,00	: : : : : : : : : : : : : : : : : : : :		organs, asthma and allergy.
 HAIB071	896	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well	A highly preferred embodiment of the invention
			known in the art and may be used or routinely modified to	includes a method for stimulating endothelial cell
			assess the ability of polypeptides of the invention	growth. An alternative highly preferred embodiment of the

	(including antibodies and	invention includes a method
	agonists or antagonists of the	for inhibiting endothelial cell
	invention) to promote caspase	growth. A highly preferred
	protease-mediated apoptosis.	embodiment of the invention
	Induction of apoptosis in	includes a method for
	endothelial cells supporting the	stimulating endothelial cell
	vasculature of tumors is	proliferation. An alternative
	associated with tumor	highly preferred embodiment
 	regression due to loss of tumor	of the invention includes a
	blood supply. Exemplary	method for inhibiting
 	assays for caspase apoptosis	endothelial cell proliferation.
	that may be used or routinely	A highly preferred
 	modified to test capase	embodiment of the invention
	apoptosis activity of	includes a method for
	polypeptides of the invention	stimulating apoptosis of
	(including antibodies and	endothelial cells. An
	agonists or antagonists of the	alternative highly preferred
	invention) include the assays	embodiment of the invention
 	disclosed in Lee et al., FEBS	includes a method for
	Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
	Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
	209-218 (2000); and Karsan	A highly preferred
	and Harlan, J Atheroscler	embodiment of the invention
 	Thromb 3(2): 75-80 (1996);	includes a method for
	the contents of each of which	stimulating angiogenisis. An
	are herein incorporated by	alternative highly preferred
	reference in its entirety.	embodiment of the invention
	Endothelial cells that may be	includes a method for
	used according to these assays	inhibiting angiogenesis. A
	are publicly available (e.g.,	highly preferred embodiment
	through commercial sources).	of the invention includes a

method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the includes	of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include	neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system	(e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular	regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy,	intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or	as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels
Exemplary endothelial cells that may be used according to these assays include bovine	dortic endothenal cents (bAEC), which are an example of endothelial cells which line blood vessels and are involved	in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immine cell extravasation				

such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that	stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or	Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications	include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma,	haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as,
			,	

pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),
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implant fixation scarring	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmine diseases (e.g.,
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lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly
	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that
	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).
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_		may be used or routinely	preferred indications include
	<u>u</u>	modified to test NFAT-	inflammation and
	-	response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
		agonists or antagonists of the	infectious disease as described
	<u></u>	invention) include assays	below under "Infectious
		disclosed in Berger et al., Gene	Disease"). Preferred
	<u> </u>	66:1-10 (1998); Cullen and	indications include neoplastic
		Malm, Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988);	"Hyperproliferative
	7	Aramburu et al., J Exp Med	Disorders"). Preferred
		182(3):801-810 (1995); De	indications include neoplasms
		Boer et al., Int J Biochem Cell	and cancers, such as, for
		Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
		Fraser et al., Eur J Immunol	and prostate, breast, lung,
		29(3):838-844 (1999); and	colon, pancreatic, esophageal,
		Yeseen et al., J Biol Chem	stomach, brain, liver and
		268(19):14285-14293 (1993),	urinary cancer. Other preferred
		the contents of each of which	indications include benign
		are herein incorporated by	dysproliferative disorders and
		reference in its entirety. NK	pre-neoplastic conditions, such
		cells that may be used	as, for example, hyperplasia,
		according to these assays are	metaplasia, and/or dysplasia.
		publicly available (e.g.,	Preferred indications also
		through the ATCC).	include anemia, pancytopenia,
		Exemplary human NK cells	leukopenia, thrombocytopenia,
		that may be used according to	Hodgkin's disease, acute
		these assays include the NK-	lymphocytic anemia (ALL),

plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis,
YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be
·	Production of IFNgamma using a T cells
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			1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	infantions associated with
			used of routiliery inodiffed to	IIIIculoiis associated with
			assess the ability of	chronic granulomatosus
			polypeptides of the invention	disease and malignant
			(including antibodies and	osteoporosis, and/or as
			agonists or antagonists of the	described below under
			invention) to mediate	"Infectious Disease"). Highly
			immunomodulation, regulate	preferred indications include
			inflammatory activities,	autoimmune disease (e.g.,
-			modulate TH2 helper cell	rheumatoid arthritis, systemic
			function, and/or mediate	lupus erythematosis, multiple
			humoral or cell-mediated	sclerosis and/or as described
			immunity. Exemplary assays	below), immunodeficiency
			that test for	(e.g., as described below),
		-	immunomodulatory proteins	boosting a T cell-mediated
			evaluate the production of	immune response, and
			cytokines, such as Interferon	suppressing a T cell-mediated
			gamma (IFNg), and the	immune response. Additional
			activation of T cells. Such	highly preferred indications
			assays that may be used or	include inflammation and
			routinely modified to test	inflammatory disorders.
			immunomodulatory activity of	Additional preferred
			polypeptides of the invention	indications include idiopathic
			(including antibodies and	pulmonary fibrosis. Highly
			agonists or antagonists of the	preferred indications include
			invention) include the assays	neoplastic diseases (e.g.,
	•		disclosed in Miraglia et al., J	leukemia, lymphoma,
			Biomolecular Screening 4:193-	melanoma, and/or as described
			204 (1999); Rowland et al.,	below under
			"Lymphocytes: a practical	"Hyperproliferative
			approach" Chapter 6:138-160	Disorders"). Highly preferred
			(2000); Gonzalez et al., J Clin	indications include neoplasms

S S S				
	embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of GM-CSF.	Highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., as described below under "Infectious Disease".  Highly preferred indications	neutropenia (and the prevention of neutropenia (e.g., in HIV infected patients), and/or as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications also include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
CSF	expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes-macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and	macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine.	Assays for immunomodulatory proteins that promote the production of GM-CSF are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	immunomodulation and modulate the growth and differentiation of leukocytes. Exemplary assays that test for immunomodulatory proteins
	CSF			
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		evaluate the production of	immunodeficiencies (e.g., as
		cytokines, such as GM-CSF,	described below). Additional
		and the activation of T cells.	highly preferred indications
-		Such assays that may be used	include asthma. Highly
		 or routinely modified to test	preferred indications include
		immunomodulatory activity of	neoplastic diseases (e.g.,
		polypeptides of the invention	leukemia (e.g., acute
		(including antibodies and	lymphoblastic leukemia, and
		agonists or antagonists of the	acute myelogenous leukemia),
		invention) include the assays	lymphoma (e.g., non-
		disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
		Biomolecular Screening 4:193-	Hodgkin"s disease), and/or as
	41-	204 (1999); Rowland et al.,	described below under
		"Lymphocytes: a practical	"Hyperproliferative
		approach" Chapter 6:138-160	Disorders"). Highly preferred
		(2000); and Ye et al., J Leukoc	indications include neoplasms
		Biol (58(2):225-233, the	and cancers, such as, leukemia,
		contents of each of which are	lymphoma, melanoma, and
		herein incorporated by	prostate, breast, lung, colon,
		reference in its entirety.	pancreatic, esophageal,
		Natural killer cells that may be	stomach, brain, liver and
		used according to these assays	urinary cancer. Other preferred
		are publicly available (e.g.,	indications include benign
		through the ATCC) or may be	dysproliferative disorders and
		isolated using techniques	pre-neoplastic conditions, such
		disclosed herein or otherwise	as, for example, hyperplasia,
		known in the art. Natural	metaplasia, and/or dysplasia.
		killer (NK) cells are large	Highly preferred indications
		granular lymphocytes that have	include: suppression of
		cytotoxic activity but do bind	immune reactions to
		antigen. NK cells show	transplanted organs and tissues

				antibody-independent killing	(e.g., bone marrow transplant);
				of tumor cells and also	accelerating myeloid recovery;
				recognize antibody bound on	and mobilizing hematopoietic
				target cells, via NK Fc	progenitor cells. Preferred
				receptors, leading to cell-	indications include boosting a
				mediated cytotoxicity.	T cell-mediated immune
_					response, and alternatively,
					suppressing a T cell-mediated
					immune response. Preferred
					indications include anemia,
					pancytopenia, leukopenia,
					thrombocytopenia, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutrophilia,
					psoriasis, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease, and
					allergy.
	HAICP19	970	Activation of	Kinase assay. Kinase assays,	A highly preferred
22			Adipocyte PI3	for example an GSK-3 assays,	embodiment of the invention
			Kinase Signalling	for PI3 kinase signal	includes a method for
			Pathway	transduction that regulate	increasing adipocyte survival
-				glucose metabolism and cell	An alternative highly preferred
				survival are well-known in the	embodiment of the invention
				art and may be used or	includes a method for
				routinely modified to assess	decreasing adipocyte survival.

	the	the ability of polypeptides of	A preferred embodiment of the
 	the	the invention (including	invention includes a method
 -	tae -	antibodies and agonists or	for stimulating adinocyte
		incource and agomets of	ior summaring ampocyte
	ant	antagonists of the invention) to	proliferation. An alternative
	pro	promote or inhibit glucose	highly preferred embodiment
	me	metabolism and cell survival.	of the invention includes a
	Ex	Exemplary assays for PI3	method for inhibiting
	kin	kinase activity that may be	adipocyte proliferation. A
-	ense	used or routinely modified to	preferred embodiment of the
	tes	test PI3 kinase-induced activity	invention includes a method
	[ Jo	of polypeptides of the	for stimulating adipocyte
_	vni	invention (including antibodies	differentiation. An alternative
	and	and agonists or antagonists of	highly preferred embodiment
	the	the invention) include assays	of the invention includes a
	dis	disclosed in Forrer et al., Biol	method for inhibiting
	Ch	Chem 379(8-9):1101-1110	adipocyte differentiation.
	(15	(1998); Nikoulina et al.,	Highly preferred indications
	Dig	Diabetes 49(2):263-271	include endocrine disorders
	(20	(2000); and Schreyer et al.,	(e.g., as described below under
 	Die	Diabetes 48(8):1662-1666	"Endocrine Disorders").
	(15	(1999), the contents of each of	Preferred indications include
	wh	which are herein incorporated	neoplastic diseases (e.g.,
	by by	by reference in its entirety.	lipomas, liposarcomas, and/or
	Me	Mouse adipocyte cells that	as described below under
	ma	may be used according to these	"Hyperproliferative
_	ass	assays are publicly available	Disorders"), blood disorders
	(e.g	(e.g., through the ATCC).	(e.g., hypertension, congestive
	Ex	Exemplary mouse adipocyte	heart failure, blood vessel
 	cel	cells that may be used	blockage, heart disease, stroke,
	acc	according to these assays	impotence and/or as described
	inc	include 3T3-L1 cells. 3T3-L1	below under "Immune

Activity", "Cardiovascular Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), and	infection (e.g., as described	below under "Infectious	Disease"). A highly	preferred indication is diabetes	mellitus. An additional	highly preferred indication is a	complication associated with	diabetes (e.g., diabetic	retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel
is an adherent mouse preadipocyte cell line that is a	continous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.																						
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weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Highly preferred	indications include neoplasms	and cancer, such as, lipoma,	liposarcoma, lymphoma,	leukemia and breast, colon,	and kidney cancer. Additional	highly preferred indications	include melanoma, prostate,	lung, pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Other preferred	indications include benign
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dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
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	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or
	Production of ICAM-1
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	HAICP19
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	ications ma, and preferred	isease as	), and	ers.	ers (e.g.,	inder .	"Blood- and/or	orders").	s include	s (e.g.,	systemic	, multiple escribed		(e.g., as	referred	neoplastic	mia,
	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred	(e.g., an infectious disease as described below under	"Infectious Disease"), and inflammation and	inflammatory disorders.  Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood- Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,
may be routinely generated.  Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1	numan mast cent line. Activation of NFAT in mast cells has been linked to	cytokine and chemokine production. Assays for the	activation of transcription	Activated T cells (NFAT)	response element are well-	known in the art and may be used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFA1	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the
	Activation of transcription through NFAT	response element in immune cells (such as mast cells).															
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	HAICP19																
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lymphoma, melanoma, prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.
NFAT response element that may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	Biol Chem 270(27):16333-	16338 (1995), and Turner et	al., J Exp Med 188:527-537	(1998), the contents of each of	which are herein incorporated	by reference in its entirety.	Mast cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to
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these assays include the HMC- 1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal assay, for ERK signal proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of includes a method for stimulating natural inhibit cell proliferation, and differentiation. Exemplary assays for ERK inase activity that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) include the
	Activation of Natural Killer Cell ERK Signaling Pathway.
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	HAICP19
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(e.g., as described below under "Immune Activity", "Cardiovascular Disorders",	and/or "Blood-Related Disorders"), immune disorders			indications inc	disorders (e.g., as described	below under "Immune Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,	breast, lung, colon, pancreatic,
al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48	(1999); Chang and Karin, Nature 410(6824):37-40 (2001): and Cobb MH. Proo	Biophys Mol Biol 71(3-4):479-500 (1999); the contents of	each of which are herein	entirety. Natural killer cells	that may be used according to	these assays are publicly available (e.g., through the	ATCC). Exemplary natural	killer cells that may be used	according to these assays	include the human natural	killer cell lines (for example,	NK-YT cells which have	cytolytic and cytotoxic	activity) or primary NK cells.									
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1 liver, urinary cancer,					esophageal, stomach, brain.
971 Activation of Kinase assay. Kinase assays, for example an Elk-1 kinase Signaling Pathway transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					liver, urinary cancer,
971 Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					lymphoma and leukemias.
971 Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					Other preferred indications
971 Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					include benign dysproliferative
971 Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					disorders and pre-neoplastic
971 Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					conditions, such as, for
971 Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					example, hyperplasia,
Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					metaplasia, and/or dysplasia.
Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					Other highly preferred
Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					indications include,
Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the				,	pancytopenia, leukopenia,
971 Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					leukemias, Hodgkin's disease,
Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					acute lymphocytic anemia
Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					(ALL), arthritis, asthma,
Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					AIDS, granulomatous disease,
Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					inflammatory bowel disease,
Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					sepsis, psoriasis, immune
Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					reactions to transplanted
Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					organs and tissues,
Adipocyte ERK for example an Elk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the					endocarditis, meningitis, Lyme
Adipocyte ERK Signaling Pathway Signaling Pathway Activation of may be used or routinely modified to assess the ability of polypeptides of the					Disease, and allergies.
for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the	HAIFL18	971	Activation of	Kinase assay. Kinase assays,	A highly preferred
assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
		,	Signaling Pathway	assay, for ERK signal	includes a method for
c				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A

	invention (including antibodies	highly preferred embodiment
	and agonists or antagonists of	of the invention includes a
	the invention) to promote or	method for stimulating
	inhibit cell proliferation,	adipocyte differentiation. An
	activation, and differentiation.	alternative highly preferred
	Exemplary assays for ERK	embodiment of the invention
-	kinase activity that may be	includes a method for
	used or routinely modified to	inhibiting adipocyte
	test ERK kinase-induced	differentiation. A highly
	activity of polypeptides of the	preferred embodiment of the
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood

disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under	"Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under	"Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"),	and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An	indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure,	nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage
(e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1	is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and	undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.			

(e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental	nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g.,	microvascular disease, microvascular disease, hypertension, stroke, and other diseases and disorders as	described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine Disorders" section below),	(e.g., diabetic retinopathy and	bindness), ulcers and impaired wound healing, infection (e.g., infection)	disorders as described in the "Infections Diseases" section	below (particularly of the	urinary tract and skin). An additional highly preferred indication is obesity and/or
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liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metanlasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as	described below under
	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	agonists or antagonists of the
	Production of IFNgamma using a T cells	
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			invention) to mediate	"Infectious Disease"). Highly
		<del></del>	immunomodulation, regulate	preferred indications include
			inflammatory activities,	autoimmune disease (e.g.,
	4.49		modulate TH2 helper cell	rheumatoid arthritis, systemic
			function, and/or mediate	lupus erythematosis, multiple
			humoral or cell-mediated	sclerosis and/or as described
			immunity. Exemplary assays	below), immunodeficiency
			that test for	(e.g., as described below),
			immunomodulatory proteins	boosting a T cell-mediated
			evaluate the production of	immune response, and
		-71,10	cytokines, such as Interferon	suppressing a T cell-mediated
			gamma (IFNg), and the	immune response. Additional
			activation of T cells. Such	highly preferred indications
			assays that may be used or	include inflammation and
			routinely modified to test	inflammatory disorders.
			immunomodulatory activity of	Additional preferred
-			polypeptides of the invention	indications include idiopathic
			(including antibodies and	pulmonary fibrosis. Highly
			agonists or antagonists of the	preferred indications include
			invention) include the assays	neoplastic diseases (e.g.,
			disclosed in Miraglia et al., J	leukemia, lymphoma,
			Biomolecular Screening 4:193-	melanoma, and/or as described
			204 (1999); Rowland et al.,	below under
			"Lymphocytes: a practical	"Hyperproliferative
			approach" Chapter 6:138-160	Disorders"). Highly preferred
			(2000); Gonzalez et al., J Clin	indications include neoplasms
			Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
	<del></del>		Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
			Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
			et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
			15:749-795 (1997), and	esophageal, stomach, brain,

the preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.  Preferred indications include		organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha r
Kneumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using	techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or
		Activation of transcription through serum response element in immune cells (such
		971
		HAIFL18
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	cells)	the ability of polypeptides of	of the invention includes a
		the invention (including	method for stimulating (e.g.,
		antibodies and agonists or	increasing) TNF alpha
-		antagonists of the invention) to	production. Preferred
	-74	regulate serum response	indications include blood
		factors and modulate the	disorders (e.g., as described
	,	expression of genes involved	below under "Immune
		in growth and upregulate the	Activity", "Blood-Related
		function of growth-related	Disorders", and/or
		genes in many cell types.	"Cardiovascular Disorders"),
		Exemplary assays for	Highly preferred indications
		transcription through the SRE	include autoimmune diseases
		that may be used or routinely	(e.g., rheumatoid arthritis,
		modified to test SRE activity	systemic lupus erythematosis,
		of the polypeptides of the	Crohn"s disease, multiple
		invention (including antibodies	sclerosis and/or as described
		and agonists or antagonists of	below), immunodeficiencies
		the invention) include assays	(e.g., as described below),
		disclosed in Berger et al., Gene	boosting a T cell-mediated
		66:1-10 (1998); Cullen and	immune response, and
		Malm, Methods in Enzymol	suppressing a T cell-mediated
		216:362-368 (1992); Henthorn	immune response. Additional
		et al., Proc Natl Acad Sci USA	highly preferred indications
		85:6342-6346 (1988); Benson	include inflammation and
		et al., J Immunol 153(9):3862-	inflammatory disorders, and
		3873 (1994); and Black et al.,	treating joint damage in
		Virus Genes 12(2):105-117	patients with rheumatoid
		(1997), the content of each of	arthritis. An additional highly
		which are herein incorporated	preferred indication is sepsis.
		by reference in its entirety. T	Highly preferred indications
		cells that may be used	include neoplastic diseases

(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and cancers, such as, for example, lenkemia lymphoma	melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis,
according to these assays are publicly available (e.g., through the ATCC).	used according to these assays include the NK-YT cell line, which is a human natural killer cell line with evtolvtic and	cytotoxic activity.				

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suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E - antigen, promoted by T helper cell type 2 cytokines, is an important component of
	Regulation of apoptosis of immune cells (such as mast cells).
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allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.	Immune cells that may be used	according to these assays are	publicly available (e.g.,	through commercial sources).	Exemplary immune cells that
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				assays include mast cells such	
_		*		as the HMC human mast cell	
				line.	
	HAJAF57	972	Activation of	Kinase assay. JNK kinase	A highly preferred
24			Endothelial Cell	assays for signal transduction	embodiment of the invention
			JNK Signaling	that regulate cell proliferation,	includes a method for
			Pathway.	activation, or apoptosis are	stimulating endothelial cell
				well known in the art and may	growth. An alternative highly
				be used or routinely modified	preferred embodiment of the
				to assess the ability of	invention includes a method
				polypeptides of the invention	for inhibiting endothelial cell
				(including antibodies and	growth. A highly preferred
				agonists or antagonists of the	embodiment of the invention
				invention) to promote or	includes a method for
				inhibit cell proliferation,	stimulating endothelial cell
		1770		activation, and apoptosis.	proliferation. An alternative
				Exemplary assays for JNK	highly preferred embodiment
				kinase activity that may be	of the invention includes a
				used or routinely modified to	method for inhibiting
				test JNK kinase-induced	endothelial cell proliferation.
				activity of polypeptides of the	A highly preferred
		-		invention (including antibodies	embodiment of the invention
			-	and agonists or antagonists of	includes a method for
				the invention) include the	stimulating apoptosis of
				assays disclosed in Forrer et	endothelial cells. An
				al., Biol Chem 379(8-9):1101-	alternative highly preferred
				[ 1110 (1998); Gupta et al., Exp	embodiment of the invention
				Cell Res 247(2): 495-504	includes a method for
				(1999); Kyriakis JM, Biochem	inhibiting apoptosis of
				Soc Symp 64:29-48 (1999);	endothelial cells. A

Chang and Karin, Nature highly preferred embodiment	and	Cobb MH, Prog Biophys Mol   method for stimulating	Biol 71(3-4):479-500 (1999); endothelial cell activation. An	the contents of each of which alternative highly preferred	are herein incorporated by embodiment of the invention	reference in its entirety.	Endothelial cells that may be inhibiting the activation of	used according to these assays and/or inactivating endothelial	 through the ATCC). embodiment of the invention	Exemplary endothelial cells includes a method for	that may be used according to stimulating angiogenisis. An	these assays include human alternative highly preferred	ells	(HUVEC), which are includes a method for	endothelial cells which line inhibiting angiogenesis. A	venous blood vessels, and are highly preferred embodiment	involved in functions that of the invention includes a	include, but are not limited to, method for reducing cardiac	angiogenesis, vascular hypertrophy. An alternative	permeability, vascular tone, highly preferred embodiment	and immune cell extravasation. of the invention include a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	- :- ::

(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications
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include antiangiogenic activity	to treat solid tumors,	corroms and retinal disorders	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery
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disease, inflammatory vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph
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angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple	below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain

					management.
	HAJBR69	973	Regulation of	Assays for the regulation of	A highly preferred
25			transcription	transcription through the	indication is diabetes mellitus.
			through the PEPCK	PEPCK promoter are well-	An additional highly preferred
			promoter in	known in the art and may be	indication is a complication
			hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the	diseases and disorders as
		-2-		PEPCK promoter in a reporter	described in the "Renal
				construct and regulate liver	Disorders" section below),
				gluconeogenesis. Exemplary	diabetic neuropathy, nerve
				assays for regulation of	disease and nerve damage
				transcription through the	(e.g., due to diabetic
				PEPCK promoter that may be	neuropathy), blood vessel
				used or routinely modified to	blockage, heart disease, stroke,
_				test for PEPCK promoter	impotence (e.g., due to diabetic
				activity (in hepatocytes) of	neuropathy or blood vessel
				polypeptides of the invention	blockage), seizures, mental
-				(including antibodies and	confusion, drowsiness,
-				agonists or antagonists of the	nonketotic hyperglycemic-
			A1 8 ***	invention) include assays	hyperosmolar coma,
				disclosed in Berger et al., Gene	cardiovascular disease (e.g.,
				66:1-10 (1998); Cullen and	heart disease, atherosclerosis,
				Malm, Methods in Enzymol	microvascular disease,
				216;362-368 (1992); Henthorn	hypertension, stroke, and other
				et al., Proc Natl Acad Sci USA	diseases and disorders as
				85:6342-6346 (1988);	described in the
				Lochhead et al., Diabetes	"Cardiovascular Disorders"

section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	blindness), ulcers and impaired wound healing, infection (e.g., an infectious diseases or disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture).  An additional highly preferred	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.
49(6):896-903 (2000); and Yeagley et al., J Biol Chem 275(23):17814-17820 (2000), the contents of each of which is herein incorporated by	Hepatocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary liver hepatoma cells that may be used according to these assays include H4lle cells, which contain a tyrosine amino	transferase that is inducible with glucocorticoids, insulin, or cAMP derivatives.

	Additional highly preferred indications include glycogen storage disease (e.g.	glycogenoses), hepatitis,	liver, degenerative or necrotic	liver disease, alcoholic liver	regeneration, metabolic	disease, dyslipidemia and	cholesterol metabolism, and	hepatocarcinomas.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), infection	(e.g., an infectious disease	and/or disorder as described	below under "Infectious	Disease"), endocrine disorders	(e.g., as described below under	"Endocrine Disorders"), and	neural disorders (e.g., as	described below under "Neural	Activity and Neurological	Diseases").

					Additional preferred
					indications include neoplastic
					diseases (e.g., as described
					below under
					"Hyperproliferative
					Disorders"). Preferred
					indications include neoplasms
					and cancers, such as, leukemia,
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					and urinary cancer. A highly
					preferred indication is liver
					cancer. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
- 1					metaplasia, and/or dysplasia.
	HAJBR69	973	Production of GM-	GM-CSF FMAT. GM-CSF is	A highly preferred
			CSF	expressed by activated T cells,	embodiment of the invention
				macrophages, endothelial cells,	includes a method for
				and fibroblasts. GM-CSF	stimulating the production of
				regulates differentiation and	GM-CSF. An alternative
	-			proliferation of granulocytes-	highly preferred embodiment
				macrophage progenitors and	of the invention includes a
				enhances antimicrobial activity	method for inhibiting the
				in neutrophils, monocytes and	production of GM-CSF.
				macrophage. Additionally,	Highly preferred indications
				GM-CSF plays an important	include inflammation and
				role in the differentiation of	inflammatory disorders. An

dendritic cells and monocytes,	additional highly preferred
and increases antigen	indication is infection (e.g., as
nresentation GM-CSF is	described below under
 considered to be a	"Infectious Disease".
proinflammatory cytokine.	Highly preferred indications
Assays for immunomodulatory	include blood disorders (e.g.,
proteins that promote the	neutropenia (and the
production of GM-CSF are	prevention of neutropenia
well known in the art and may	(e.g., in HIV infected patients),
be used or routinely modified	and/or as described below
to assess the ability of	under "Immune Activity",
polypeptides of the invention	"Blood-Related Disorders",
(including antibodies and	and/or "Cardiovascular
agonists or antagonists of the	Disorders"). Highly preferred
invention) to mediate	indications also include
 immunomodulation and	autoimmune diseases (e.g.,
modulate the growth and	rheumatoid arthritis, systemic
differentiation of leukocytes.	lupus erythematosis, multiple
Exemplary assays that test for	sclerosis and/or as described
immunomodulatory proteins	below) and
evaluate the production of	immunodeficiencies (e.g., as
cytokines, such as GM-CSF,	described below). Additional
and the activation of T cells.	highly preferred indications
Such assays that may be used	include asthma. Highly
or routinely modified to test	preferred indications include
immunomodulatory activity of	neoplastic diseases (e.g.,
polypeptides of the invention	leukemia (e.g., acute
(including antibodies and	lymphoblastic leukemia, and
 agonists or antagonists of the	acute myelogenous leukemia),
invention) include the assays	lymphoma (e.g., non-
disclosed in Miraglia et al., J	Hodgkin"s lymphoma and

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Hodgkin"s disease), and/or as described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	include: suppression of	immune reactions to	transplanted organs and tissues	(e.g., bone marrow transplant);	accelerating myeloid recovery;	and mobilizing hematopoietic	progenitor cells. Preferred	indications include boosting a	T cell-mediated immune	response, and alternatively,	suppressing a T cell-mediated	immune response. Preferred	indications include anemia,	pancytopenia, leukopenia,
Hordes	(H.,	Dis	jud	and	$  \log r$	pro	pan	stoi	uri	ind	dys	pre	as,	me	Hig	inc	imi	trar	(e.£	acc	and	pro	jind	Tc	res	dns	ımı	jud	pan
Biomolecular Screening 4:193-204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Ye et al., J Leukoc	Biol (58(2):225-233, the	contents of each of which are	herein incorporated by	reference in its entirety.	Natural killer cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) or may be	isolated using techniques	disclosed herein or otherwise	known in the art. Natural	killer (NK) cells are large	granular lymphocytes that have	cytotoxic activity but do bind	antigen. NK cells show	antibody-independent killing	of tumor cells and also	recognize antibody bound on	target cells, via NK Fc	receptors, leading to cell-	mediated cytotoxicity.					
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				thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, psoriasis, hemophilia, mellitus, endocarditis, meningitis, Lyme Disease, and alleroy.
HAJBZ75	974	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative

			1	GAS-response element activity   disorders and pre-neoplastic	disorders and pre-neoplastic
				of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
	_, <u>,</u>	<del>.</del>		and agonists or antagonists of	metaplasia, and/or dysplasia.
				the invention) include assays	Preferred indications include
				disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
				66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
				Malm, Methods in Enzymol	lupus erythematosis, multiple
-		<del></del>		216:362-368 (1992); Henthorn	sclerosis and/or as described
				et al., Proc Natl Acad Sci USA	below), immunodeficiencies
		<del></del>		85:6342-6346 (1988);	(e.g., as described below),
				Matikainen et al., Blood	boosting a T cell-mediated
				93(6):1980-1991 (1999); and	immune response, and
		**		Henttinen et al., J Immunol	suppressing a T cell-mediated
				155(10):4582-4587 (1995), the	immune response. Additional
		•		contents of each of which are	preferred indications include
				herein incorporated by	inflammation and
		,		reference in its entirety.	inflammatory disorders.
				Exemplary human T cells,	Highly preferred indications
		• •		such as the SUPT cell line, that	include blood disorders (e.g.,
				may be used according to these	as described below under
_		-		assays are publicly available	"Immune Activity", "Blood-
		-		(e.g., through the ATCC).	Related Disorders", and/or
					"Cardiovascular Disorders"),
					and infection (e.g., viral
					infections, tuberculosis,
					infections associated with
-					chronic granulomatosus
					disease and malignant
		-			osteoporosis, and/or an
					infectious disease as described

below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include	anemia, pancytopenia, leukopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,	su s	Assays for the activation of transcription through the nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies).  Highly preferred indications include autoimmune diseases invention (including antibodies).
			Activation of transcription through NFAT response element in immune cells (such as T-cells).
			974
			HAJBZ75
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multiple sclerosis and/or as described below), immimodeficiencies (e.g. as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Additional highly	preferred indications include	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Disease"). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dvsproliferative disorders and
the invention) to regulate  NFAT transcription factors and	modulate expression of genes involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta	1498(1):1-18 (2000); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by
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pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell	line, which is a suspension culture of IL-2 and IL-4 responsive T cells.		Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays
			Production of ICAM-1
		and the second s	975
			HAMFK58
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ly  -1   t   t   t   t   t   t   t   e   e   e   e   e   e   ays   e   e   e   e   e   e   e   e   e   e	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell
that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	<u> </u>
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	HAMGG68
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proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting	endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for	stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention	includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells.	A highly preferred embodiment of the invention includes a method for stimulating (e.g. increasing)	endothelial cell activation. An alternative highly preferred embodiment of the invention	includes a method for inhibiting (e.g., decreasing) the activation of and/or inactivating endothelial cells.	
proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or	routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include the assays disclosed in Forrer et	a., Dio (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and	Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by	reference in its entirety.  Endothelial cells that may be used according to these assays are publicly available (e.g.,	through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells
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embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	 method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").
(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.	 -																·					
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Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic	disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels	themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or	cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications	include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications	such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma,
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lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as,	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis,	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and	thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as

wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions),	implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal	failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or	and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment	/prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and	vascular disease.  Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-

Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under
	Endothelial cells, which are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used in ICAM production assays include human umbilical vein endothelial cells (HUVEC), and are available from
	Production of ICAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
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	HAMGG68
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	commercial sources. The	"Immune Activity", "Blood-
	expression of ICAM (CD54),a	Related Disorders",
	intergral memorane protein,	"Hyperproliferative Disorders"
	cytokines or other factors and	allu/ol Calulovasculal Disorders" Highly preferred
	ICAM expression is important	indications include neoplasms
	in mediating immune and	and cancers such as, for
	endothelial cell interactions	example, leukemia, lymphoma,
	leading to immune and	melanoma, renal cell
	inflammatory responses.	carcinoma, and prostate,
	Assays for measuring	breast, lung, colon, pancreatic,
· O DANGE	expression of ICAM-1 are	esophageal, stomach, brain,
	well-known in the art and may	liver and urinary cancer. Other
	be used or routinely modified	preferred indications include
	to assess the ability of	benign dysproliferative
	polypeptides of the invention	disorders and pre-neoplastic
	(including antibodies and	conditions, such as, for
	agonists or antagonists of the	example, hyperplasia,
	invention) to regulate ICAM-1	metaplasia, and/or dysplasia.
	expression. Exemplary assays	
	that may be used or routinely	
	modified to measure ICAM-1	
	expression include assays	
	disclosed in: Rolfe BE, et al.,	
	Atherosclerosis, 149(1):99-110	
	(2000); Panettieri RA Jr, et al.,	
	J Immunol, 154(5):2358-2365	
	(1995); and, Grunstein MM, et	
	al., Am J Physiol Lung Cell	
	Mol Physiol, 278(6):L1154-	
	L1163 (2000), the contents of	

53	HANGG89	977	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	each of which is herein incorporated by reference in its entirety.  This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line.  Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia.
				routinely modified to test GATA3-response element activity of polypeptides of the	lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal.

stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.			
invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to	these assays include the HMC-	1 cell line, which is an	immature human mast cell line	established from the peripheral	blood of a patient with mast
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				cell leukemia, and exhibits many characteristics of immature mast cells.	
29	HANGG89	717	Activation of transcription	This reporter assay measures activation of the NFAT	Highly preferred indications include allergy, asthma, and
<b>\</b>			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in immune cells (such	human mast cell line. Activation of NFAT in mast	indications include infection (e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
			`	cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
		~~~		through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
	· ·			polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
		***		agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
				transcription through the	diseases (e.g., leukemia,
				NFAT response element that	lymphoma, melanoma,
				may be used or routinely	prostate, breast, lung, colon,
				modified to test NFAT-	pancreatic, esophageal,

		or as			red	7	and	snch	sia,	sia.	nde		enia,	ease,	et		tt's	s,		ase,		•			philia,	Se		sease.			
liver and	11 VC1, cult.	cers and/	under	ive	her prefe	de benig	disorders	onditions	hyperpla	or dyspla	tions incl	penia,	mbocyto	zkin's dis	tic anemi	ytomas,	na, Burki	ritis, AID	lisease,	wel dise	nia,	oriasis,	mmune	splanted	es, hemo	n, diabet	ırditis,	Lyme Di			
ctomach brain liver and	11, Otalli,	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.			
otomoto	stolliat.	urinary	describ	"Hyper	Disord	indicati	dyspro	pre-nec	as, for	metapl	Preferr	anemia	leukop	leuken	acute 1	(ALL),	multip	lymphe	granule	inflam	sepsis,	neutrol	suppre	reactio	organs	hyperc	mellitu	mening			
44, 06	17 VI	ention	nd	of the	ys	il., Gene	and	ymol	enthorn	Sci USA	De Boer	ell Biol	9); Ali		(00)	skey, J	333-	ner et	7-537	each of	porated	rety.	nsed	ys are	ŗ		st cells	ding to	e HMC-		• • • • • • • • • • • • • • • • • • • •
ont portix		of the inv	ibodies a	tagonists	lude assa	erger et a	); Cullen	ds in Enz	1992); H	Itl Acad S	(1988);	ochem Co	1236 (199	lou	-7223 (20	nd McClc	(0(27):16	, and Tur	1188:527	ntents of	ein incor	n its enti	t may be	hese assa	able (e.g.	TCC).	ıman mas	sed accor	nclude th	ich is an	
mole of	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	Biol Chem 270(27):16333-	16338 (1995), and Turner et	al., J Exp Med 188:527-537	(1998), the contents of each of	which are herein incorporated	by reference in its entirety.	Mast cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to	these assays include the HMC-	1 cell line, which is an	
	odsot	polyp	(inclu	agoni	inven	discle	66:1-	Maln	216:3	et al.,	85:63	et al.	31(10	et al.	165(	Hutc	Biol	1633	al., J	(199	whic	by re	Mast	accol	ldud	throu	Exen	that 1	these	1 cel	-
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						•	•	•																	-						
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			established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	
HAPBS03	826	Activation of Adipocyte ERK	Kinase assay. Kinase assays, for example an Elk-1 kinase	A highly preferred embodiment of the invention
		Signaling Pathway	assay, for ERK signal transduction that regulate cell	includes a method for stimulating adipocyte
			proliferation or differentiation are well known in the art and	proliferation. An alternative highly preferred embodiment
			may be used or routinely	of the invention includes a
			of polypeptides of the	adipocyte proliferation. A
			invention (including antibodies	highly preferred embodiment of the invention includes a
			the invention) to promote or	method for stimulating
			inhibit cell proliferation,	adipocyte differentiation. An
		-	activation, and differentiation.	alternative highly preferred
		g and	kinase activity that may be	includes a method for
			used or routinely modified to	inhibiting adipocyte
			test ERK kinase-induced	differentiation. A highly
			activity of polypeptides of the	preferred embodiment of the
			invention (including antibodies	invention includes a method
		···	and agonists or antagonists of	for stimulating (e.g.,
			the invention) include the assays disclosed in Forrer et	increasing) adipocyte activation. An alternative
			al., Biol Chem 379(8-9):1101-	highly preferred embodiment
			1110 (1998); Le Marchand-	of the invention includes a
			Brustel Y, Exp Clin	method for inhibiting the

		Endocrinol Diabetes	activation of (e.g., decreasing)
-		107(2)-126-132 (1999):	and/or inactivating adipocytes.
•		Kyriakis JM, Biochem Soc	Highly preferred indications
		Symp 64:29-48 (1999); Chang	include endocrine disorders
	_	and Karin, Nature	(e.g., as described below under
		410(6824):37-40 (2001); and	"Endocrine Disorders").
		Cobb MH, Prog Biophys Mol	Highly preferred indications
		Biol 71(3-4):479-500 (1999);	also include neoplastic
		the contents of each of which	diseases (e.g., lipomas,
		are herein incorporated by	liposarcomas, and/or as
		reference in its entirety.	described below under
		Mouse adipocyte cells that	"Hyperproliferative
		may be used according to these	Disorders"). Preferred
		assays are publicly available	indications include blood
		(e.g., through the ATCC).	disorders (e.g., hypertension,
		Exemplary mouse adipocyte	congestive heart failure, blood
		cells that may be used	vessel blockage, heart disease,
		according to these assays	stroke, impotence and/or as
		include 3T3-L1 cells. 3T3-L1	described below under
		is an adherent mouse	"Immune Activity",
	344	preadipocyte cell line that is a	"Cardiovascular Disorders",
		continuous substrain of 3T3	and/or "Blood-Related
		fibroblast cells developed	Disorders"), immune disorders
		through clonal isolation and	(e.g., as described below under
		undergo a pre-adipocyte to	"Immune Activity"), neural
		adipose-like conversion under	disorders (e.g., as described
		appropriate differentiation	below under "Neural Activity
		conditions known in the art.	and Neurological Diseases"),
			and infection (e.g., as
			described below under
			"Infectious Disease").

A highly preferred indication	is diabetes mellitus. An	eferre	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,
and service and se	-																													
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endocrine disorders (as	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery
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disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preterred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders.
	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of
	Activation of transcription through STAT6 response element in immune cells (such as T-cells).
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	polypeptides of the invention	Preferred indications include
	(including antibodies and	blood disorders (e.g., as
	agonists or antagonists of the	described below under
	invention) to regulate STAT6	"Immune Activity", "Blood-
	transcription factors and	Related Disorders", and/or
	modulate the expression of	"Cardiovascular Disorders").
	multiple genes. Exemplary	Preferred indications include
	assays for transcription	autoimmune diseases (e.g.,
	through the STAT6 response	rheumatoid arthritis, systemic
	element that may be used or	lupus erythematosis, multiple
	routinely modified to test	sclerosis and/or as described
	STAT6 response element	below) and
	activity of the polypeptides of	immunodeficiencies (e.g., as
	the invention (including	described below).
	antibodies and agonists or	Preferred indications include
	antagonists of the invention)	neoplastic diseases (e.g.,
	include assays disclosed in	leukemia, lymphoma,
	Berger et al., Gene 66:1-10	melanoma, and/or as described
	(1998); Cullen and Malm,	below under
	Methods in Enzymol 216:362-	"Hyperproliferative
	368 (1992); Henthorn et al.,	Disorders"). Preferred
	Proc Natl Acad Sci USA	indications include neoplasms
	85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
	et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
	(1998); Moffatt et al.,	prostate, breast, lung, colon,
	Transplantation 69(7):1521-	pancreatic, esophageal,
	1523 (2000); Curiel et al., Eur	stomach, brain, liver and
	J Immunol 27(8):1982-1987	urinary cancer. Other preferred
	(1997); and Masuda et al., J	indications include benign
	Biol Chem 275(38):29331-	dysproliferative disorders and
1 option and	29337 (2000), the contents of	pre-neoplastic conditions, such

3				each of which are herein	as, for example, hyperplasia,
				incorporated by reference in its	metaplasia, and/or dysplasia.
				entirety. T cells that may be	Preferred indications include
				used according to these assays	anemia, pancytopenia,
				are publicly available (e.g.,	leukopenia, thrombocytopenia,
				through the ATCC).	Hodgkin's disease, acute
				Exemplary T cells that may be	lymphocytic anemia (ALL),
				used according to these assays	plasmacytomas, multiple
	****			include the SUPT cell line,	myeloma, Burkitt's lymphoma,
				which is a suspension culture	arthritis, AIDS, granulomatous
				of IL-2 and IL-4 responsive T	disease, inflammatory bowel
				cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
				***************************************	suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additional preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HAPNY94	086	Activation of	Kinase assay. Kinase assays,	A highly preferred
			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a

se Disorders"). Preferred indications include blood		congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	a "Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	er disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),
may be used according to these assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.															
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diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuronathy) blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic neuronathy or blood vessel	blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis,	microvascular disease, hypertension, stroke, and other diseases and disorders as	described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine Disorders" section below), neuropathy, vision impairment	blindness), ulcers and impaired wound healing, infection (e.g., infections diseases and	disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An
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additional highly preferred indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,
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prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Kinase assay. JNK and p38  Rinase assays for signal  kinase assays for signal  kinase assays for signal  kinase assays for signal  kinase assays for signal  ransduction that regulate cell  proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell  (e.g. T-cell) proliferation, and apoptosis.  Exemplary assays for JNK and activation, and apoptosis.  By hinase activity that may be used or routinely modified to assays for JNK and p38 kinase- induced activity of induced activity of below) and
	Activation of T-Cell p38 or JNK Signaling Pathway.
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agonists or antagonists of the invention) include the assays	highly preferred indications include inflammation and
disclosed in Forrer et al., Biol	inflammatory disorders.
Chem 379(8-9):1101-1110	Highly preferred indications
(1998); Gupta et al., Exp Cell	also include neoplastic
Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	"Hyperproliferative
410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the contents of each of which	lymphoma, prostate, breast,
are herein incorporated by	lung, colon, pancreatic,
reference in its entirety. T	esophageal, stomach, brain,
cells that may be used	liver, and urinary cancer. Other
according to these assays are	preferred indications include
publicly available (e.g.,	benign dysproliferative
through the ATCC).	disorders and pre-neoplastic
Exemplary mouse T cells that	conditions, such as, for
may be used according to these	example, hyperplasia,
assays include the CTLL cell	metaplasia, and/or dysplasia.
line, which is an IL-2	Preferred indications include
dependent suspension-culture	arthritis, asthma, AIDS,
cell line with cytotoxic	allergy, anemia, pancytopenia,
activity.	leukopenia, thrombocytopenia,
	Hodgkin"s disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
de sign	myeloma, Burkitt"s lymphoma,
1	(1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.

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disease owel d s, supp tions t gans ar ditis, Lyme	red od for od for od for inclu i. An a l embc i inclu piting produc cd indi or enh nunity. ttions i tr Dison r. Bison r. Bison r. Dison r. Bison r. Dison	seases rritis, s
intory by coriasis ne reac ted org the organical is, and is, and	preferent of an anthony (e.g. function) and (e.g. function) or inhin or inhin or inhin all imm all imm all imm indices orders orders. Active orders ascula ascula ascula us Disordus bisony in orders in order	une di
granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)  IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic
gra infl infl infl of of tra tris tris	10.0	-
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to	assess the ability of polypeptides of the invention
	by Strong by Str	of of the inv
	IL-6 FMAT. IL-6 is produce by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cell. Deregulated expression of IL has been linked to autoimmudisease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulato and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, grow factors, and hormones are we known in the art and may be used or routinely modified to	assess the ability of polypeptides of the
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	IL-i lgE lgE lgA lgB	ass
	f.IL-6	
	Production of IL-6	
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	HAPQT22	
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(including antibodies and	lupus erythematosis, multiple
agonists or antagonists of the	sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
differentiation and modulate T	described below). Highly
cell proliferation and function.	preferred indications also
Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include .
proliferation and functional	inflammation and
activities. Such assays that	inflammatory
 may be used or routinely	disorders. Additional highly
modified to test	preferred indications include
immunomodulatory and	asthma and allergy. Highly
diffferentiation activity of	preferred indications include
polypeptides of the invention	neoplastic diseases (e.g.,
(including antibodies and	myeloma, plasmacytoma,
agonists or antagonists of the	leukemia, lymphoma,
 invention) include assays	melanoma, and/or as described
disclosed in Miraglia et al., J	below under
Biomolecular Screening 4:193-	"Hyperproliferative
204(1999); Rowland et al.,	Disorders"). Highly preferred
"Lymphocytes: a practical	indications include neoplasms
approach" Chapter 6:138-160	and cancers, such as, myeloma,
(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
Immunol 158:2919-2925	lymphoma, melanoma, and
 (1997), the contents of each of	prostate, breast, lung, colon,
which are herein incorporated	pancreatic, esophageal,

				by reference in its entirety.	stomach, brain, liver and
			10.0	Human dendritic cells that may	urinary cancer. Other preferred
				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
1904			•	and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
			***		neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
	***				infectious disease as described
					below under "Infectious
					Disease").
	HAPQT22	982	Production of	MCP-1 FMAT. Assays for	A highly preferred
34			MCP-1	immunomodulatory proteins	embodiment of the invention

includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred	embodiment of the invention includes a method for inhibiting (e.g., reducing)  MCP-1 production. A highly	is is paragraphic	under "Infectious Disease"). Additional highly preferred indications include	inflammation and inflammatory disorders.	Preferred indications include blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Highly preferred indications	(e.g., rheumatoid arthritis, systemic lupus erythematosis,	multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Preferred
that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T	cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the	invention (including antibodies and agonists or antagonists of the invention) to mediate	immunomodulation, induce chemotaxis, and modulate immune cell activation.	Exemplary assays that test for immunomodulatory proteins	evaluate the production of cell surface markers, such as	protein (MCP), and the activation of monocytes and T	cells. Such assays that may be used or routinely modified to	differentiation activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the	invention) include assays disclosed in Miraglia et al., J
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anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,	meningitis (bacterial and viral), Lyme Disease, asthma, and allergy Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include
204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol	158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety.  Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or	otherwise known in the art.  Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.

					benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
35	HAPUC89	983	Activation of Adipocyte ERK	Kinase assay. Kinase assays, for example an Elk-1 kinase	A highly preferred embodiment of the invention
			Signaling Pathway	assay, for ERK signal transduction that regulate cell proliferation or differentiation	includes a method for stimulating adipocyte proliferation. An alternative
				are well known in the art and may be used or routinely	highly preferred embodiment of the invention includes a
				of polypeptides of the invention (including antibodies	adipocyte proliferation. A highly preferred embodiment
				and agonists or antagonists of the invention) to promote or	of the invention includes a method for stimulating
				inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK	adipocyte differentiation. An alternative highly preferred embodiment of the invention
				kinase activity that may be used or routinely modified to	includes a method for inhibiting adipocyte
				test EKK Kinase-induced activity of polypeptides of the invention (including antibodies	differentiation. A highly preferred embodiment of the invention includes a method
				and agonists or antagonists of the invention) include the	for stimulating (e.g., increasing) adipocyte
				assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-	activation. An alternative highly preferred embodiment
				1110 (1998); Le Marchand- Brustel Y, Exp Clin	of the invention includes a method for inhibiting the

Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	activation of (e.g., decreasing)	and/or inactivating adipocytes. Highly preferred indications		(e.g., as described below under		s Mol Highly preferred indications	999); also include neoplastic	which diseases (e.g., lipomas,		described below under		o these   Disorders"). Preferred	able   indications include blood	). disorders (e.g., hypertension,		vessel blockage, heart disease,	s stroke, impotence and/or as	F3-L1   described below under	"Immune Activity",		3T3 and/or "Blood-Related		and (e.g., as described below under		under   disorders (e.g., as described	on below under "Neural Activity	art. and Neurological Diseases"),	and infection (e.g., as	described below under	
	Endocrinol Diabetes	10/(2):120-132 (1999);   Kvriakis JM. Biochem S	Symp 64:29-48 (1999);	and Karin, Nature	410(6824):37-40 (2001)	Cobb MH, Prog Biophy	Biol 71(3-4):479-500 (1	the contents of each of v	are herein incorporated	reference in its entirety.	Mouse adipocyte cells tl	may be used according t	assays are publicly avail	(e.g., through the ATCC	Exemplary mouse adipo	cells that may be used	according to these assay	include 3T3-L1 cells. 3'	is an adherent mouse	preadipocyte cell line th	continuous substrain of	fibroblast cells develope	through clonal isolation	undergo a pre-adipocyte	adipose-like conversion	appropriate differentiation	conditions known in the			
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A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication	diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as	described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia.
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w), w), w), w), with a saint and w), w), w), w), w), with a mpa on (6 dolor) w		endocrine disorders (as	lers (as
Disordera" section below)  neuropathy, vision impairmen  (e.g., diabetic retinopathy and blindness), ulcers and impaire wound healing, infection (e.g., diabetic retinopathy and blindness), ulcers and impaire wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). Arx additional highly preferred indication is obesity, Additional highly preferred indications associated with obesity. Additional highly preferred indications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or a described herein.  Additional highly preferred indications including myopathies, muscular dystrophy, and/or a described herein.  Additional highly preferred indications including myopathies, muscular dystrophy, son/or a described herein.		יילן אין דיין היילוייסטרד	"Endooring
Interceptibly, vision impairment  (e.g., diabetic retinopathy and blindness), ulcers and impaire wound healing, infection (e.g., diabetic retinopathy and blindness), ulcers and impaire wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). And additional highly preferred indications associated with obesity. Additional highly preferred indications include weight gain. Additional highly preferred indications a complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoseletal systems including myopathies, muscular dystrophy, andror a described herein.  Additional highly preferred indications including myopathies, muscular dystrophy, andror a described herein.  Additional highly preferred indications include, hypertered indications include, hypertered indications include.			Elidocillic
(e.g., diabetic rethopathy, vision impairmen (e.g., diabetic rethopathy and blindness), ulcers and impairmen infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tact and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications a complications as sociated with insulin resistance. Additional highly preferred indications includent muscular dystophy, and/or a described heterin. Additional highly preferred indications including myopathies, muscular dystophy, and/or a described heterin. Additional highly preferred indications including myopathies, muscular dystophy, and/or a described heterin. Additional highly preferred indications including myopathies, coronary artery hypertension, coronary artery		Disorders" sectio	on below),
bindness), ulcers and impaire wound healing, infection (e.g., diabetic retinopathy and disorders as described in the "Infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the univary tact and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight gain. Additional highly preferred indications include weight gain. Additional highly preferred indications associated with insulin resistance.  Additional highly preferred indications are disorders of the muscular dystrophy, and/or a described herein.  Additional highly preferred indications are disorders of the muscular dystrophy, and/or a described herein.  Additional highly preferred indications include, hyperferred indications include, hyperferred indications and a resonance and		neuropathy, visio	on impairment
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infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance. Additional highly preferred indications associated with musculoskeletal systems including myopathies, muscular dystrophy, and/or a described herein. Additional highly preferred indications include, indications include, coronary artery		wound healing, ii	infection (e.g.,
disorders as described in the  "Infectious Diseases" section below (particularly of the urinary tract and skin). Ar additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight gain. Additional highly weight gain. Additional highly preferred indications a complications associated with insulin resistance. Additional highly preferred indications are disorders of th musculoskeletal systems including myopathies, musculoskeletal systems including myopathies, musculoskeletal systems described herein. Additional highly preferred indications include, hypertension, coronary artery		infectious disease	ses and
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urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight gain. Additional highly preferred indications a complications associated with insulin resistance. Additional highly preferred indications are disorders of th musculoskeletal systems including myopathies, musculoskeletal systems including myopathies, musculoskeletal systems including myopathies, musculoskeletal systems including myopathies, hypertension, coronary artery	-	below (particular	rrly of the
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indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications a complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or a described herein.  Additional highly preferred indications include, hypertension, coronary artery		additional highly	y preferred
complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications a complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or a described herein.  Additional highly preferred indications include, hypertension, coronary artery		indication is obes	esity and/or
obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications a complication associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or a described herein.  Additional highly preferred indicational highly preferred indicational highly preferred hypertension, coronary artery		complications as	ssociated with
preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications a complications associated with insulin resistance. Additional highly preferred indications are disorders of th musculoskeletal systems including myopathies, muscular dystrophy, and/or a described herein. Additional highly preferred indications include, hypertension, coronary artery		obesity. Addition	onal highly
weight loss or alternatively, weight gain. Additional highly preferred indications a complications associated with insulin resistance. Additional highly preferred indications are disorders of th musculoskeletal systems including myopathies, muscular dystrophy, and/or a described herein. Additional highly preferred indications include, hypertension, coronary artery		preferred indicate	tions include
weight gain. Additional highly preferred indications a complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or a described herein.  Additional highly preferred indications include, hypertension, coronary artery		weight loss or alt	Iternatively,
highly preferred indications as complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or adescribed herein.  Additional highly preferred indicational highly preferred indications include, hypertension, coronary artery		weight gain.	Additional
complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or adescribed herein.  Additional highly preferred indications include, hypertension, coronary artery		highly preferred	Indications are
insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or adescribed herein.  Additional highly preferred indications include, hypertension, coronary artery		complications as	ssociated with
Additional highly preferred indications are disorders of th musculoskeletal systems including myopathies, muscular dystrophy, and/or adescribed herein.  Additional highly preferred indications include, hypertension, coronary artery		insulin resistance	e.
indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or adescribed herein.  Additional highly preferred indications include, hypertension, coronary artery		Additional highl	ly preferred
musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery		indications are di	disorders of the
including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery		musculoskeletal	l systems
muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery		including myopa	athies,
described herein. Additional highly preferred indications include, hypertension, coronary artery		muscular dystrop	ophy, and/or as
Additional highly preferred indications include,		described herein.	n.
indications include, hypertension, coronary artery		Additional highly	ly preferred
hypertension, coronary artery		indications inclu	nde,
		hypertension, co	oronary artery

					disease dyslinidemia
					golletonog ogtocouthuitie
					galistones, osteoarmins,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
					lymphoma, leukemia and
		•			breast, colon, and kidney
					cancer. Additional preferred
					indications include melanoma,
	-				prostate, lung, pancreatic,
			-		esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
			***		pre-neoplastic conditions, such
	-				as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HAPUC89	983	Activation of	This reporter assay measures	Highly preferred indications
35			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
			•	cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
		T			

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inflammatory disorders.  Preferred indications also include blood disorders (e.g., as described below under "Immine Activity", "Blood-	Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g.,	rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Preferred indications include neoplastic	diseases (e.g., leukemia, lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary tract cancers and/or as described below under "Hyperproliferative Disorders"). Other preferred	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include
activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well- known in the art and may be	used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes	involved in immunomodulatory functions. Exemplary assays for	transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988). De Boer
	James de	.,				
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				et al Int J Biochem Cell Biol	anemia nancytonenia
				31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
				et al., J Immunol	leukemias, Hodgkin's disease,
				165(12):7215-7223 (2000);	acute lymphocytic anemia
				Hutchinson and McCloskey, J	(ALL), plasmacytomas,
				Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
	_			(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
***				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
		-,		these assays include the HMC-	•
				1 cell line, which is an	
				immature human mast cell line	
_				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
!	HAPUC89	983	Activation of	Kinase assay. Kinase assays,	Highly preferred indications
35			Skeletal Muscle	for examplek Elk-1 kinase	include endocrine disorders
			Cell ERK	assays, for ERK signal	(e.g., as described below under
			Signalling Pathway	transduction that regulate cell	"Endocrine Disorders") and
				proliferation or differentiation	disorders of the
				are well known in the art and	musculoskeletal system.

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Preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), blood disorders	(e.g., as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	''Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diahetic neuronathy nerve
may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety Bat

disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel	blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis, microvascular disease.	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and
myoblast cells that may be used according to these assays are publicly available (e.g.,	through the ATCC).  Exemplary rat myoblast cells that may be used according to	these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary	cultures of rat thigh muscle, that fuses to form	multinucleated myotubes and striated fibers after culture in	differentiation media.															
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Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with	obesity. Additional highly preferred indications include weight loss or alternatively,	red inclusions associated.	indications are disorders of the musculoskeletal systems including myonathies.	muscular dystrophy, and/or as described herein.	Additional highly preferred indications include: myopathy, atrophy, congestive heart	failure, cachexia, myxomas, fibromas, congenital	cardiovascular abnormalities, heart disease, cardiac arrest,	heart valve disease, and vascular disease. Highly	neoplasms and cancer, such as,	rhabdosarcoma, stomach, esophageal, prostate, and

					urinary cancer. Highly
					preferred indications also
	-				include breast, lung, colon,
					pancreatic, brain, and liver
					cancer. Other preferred
					indications include benign
			-		dysproliferative disorders and
					pre-neoplastic conditions, such
					as, hyperplasia, metaplasia,
					and/or dysplasia.
	HASAV70	984	Production of	MIP-1alpha FMAT. Assays	A highly preferred
36			MIP1alpha	for immunomodulatory	embodiment of the invention
				proteins produced by activated	includes a method for
				dendritic cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well	embodiment of the invention
				known in the art and may be	includes a method for
				used or routinely modified to	inhibiting (e.g., reducing)
				assess the ability of	MIP1a production. A highly
				polypeptides of the invention	preferred indication is
				(including antibodies and	infection (e.g., an infectious
				agonists or antagonists of the	disease as described below
				invention) to mediate	under "Infectious Disease").
				immunomodulation, modulate	Preferred indications include
				chemotaxis, and modulate T	blood disorders (e.g., as
1				cell differentiation. Exemplary	described below under
				assays that test for	"Immune Activity", "Blood-
				immunomodulatory proteins	Related Disorders", and/or
-				evaluate the production of	"Cardiovascular Disorders").
				chemokines, such as	Highly preferred indications
				macrophage inflammatory	include autoimmune diseases

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(e.g., rheumatoid arthritis, systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below
protein 1 alpha (MIP-1a), and the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-	29 (2000); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or
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d ita, ita,	) ive t t s ent y
under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
otherwise known in the art.  Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the
	Production of IL-6
	586
	HASCG84
	37

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"Cardiovascular Disorders"),	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative
expression level is strongly	factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-
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	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
-	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,
	and/or cytokines, initiate and	Hodgkin's disease, acute
	upregulate T cell proliferation	lymphocytic anemia (ALL),
	and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
	7 Marie	meningitis, and Lyme Disease.

					An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
37	HASCG84	586	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
				macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as

described below). Additional highly preferred indications include inflammation and inflammatory disorders.  Preferred indications also	include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	piasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel	ansease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted	organs and ussues, nemopound, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy.	include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative	Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast,
test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al.,	approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb	42(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925	Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety.	be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.	Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen

				and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
38	HATAC53	986	Production of GM-CSF	GM-CSF FMAT. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes-macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine. Assays for immunomodulatory proteins that promote the production of GM-CSF are	A highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of GM-CSF. Highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indications indication is infection (e.g., as described below under "Infectious Disease". Highly preferred indications include blood disorders (e.g., neutropenia (and the prevention of neutropenia
				well known in the art and may be used or routinely modified	(e.g., in HIV infected patients), and/or as described below

		to assess the ability of	under "Immune Activity",
		polypeptides of the invention	"Blood-Related Disorders",
		(including antibodies and	and/or "Cardiovascular
		agonists or antagonists of the	Disorders"). Highly preferred
		invention) to mediate	indications also include
		immunomodulation and	autoimmune diseases (e.g.,
		modulate the growth and	rheumatoid arthritis, systemic
		differentiation of leukocytes.	lupus erythematosis, multiple
		Exemplary assays that test for	sclerosis and/or as described
		immunomodulatory proteins	below) and
		evaluate the production of	immunodeficiencies (e.g., as
		cytokines, such as GM-CSF,	described below). Additional
	-	and the activation of T cells.	highly preferred indications
		Such assays that may be used	include asthma. Highly
		or routinely modified to test	preferred indications include
		immunomodulatory activity of	neoplastic diseases (e.g.,
-8		polypeptides of the invention	leukemia (e.g., acute
		(including antibodies and	lymphoblastic leukemia, and
		agonists or antagonists of the	acute myelogenous leukemia),
		invention) include the assays	lymphoma (e.g., non-
		disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
		Biomolecular Screening 4:193-	Hodgkin"s disease), and/or as
		204 (1999); Rowland et al.,	described below under
		"Lymphocytes: a practical	"Hyperproliferative
		approach" Chapter 6:138-160	Disorders"). Highly preferred
		(2000); and Ye et al., J Leukoc	indications include neoplasms
		Biol (58(2):225-233, the	and cancers, such as, leukemia,
		contents of each of which are	lymphoma, melanoma, and
		herein incorporated by	prostate, breast, lung, colon,
		reference in its entirety.	pancreatic, esophageal,
		Natural killer cells that may be	stomach, brain, liver and

																	_			-								_
urinary cancer. Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	include: suppression of	immune reactions to	transplanted organs and tissues	(e.g., bone marrow transplant);	accelerating myeloid recovery;	and mobilizing hematopoietic	progenitor cells. Preferred	indications include boosting a	T cell-mediated immune	response, and alternatively,	suppressing a T cell-mediated	immune response. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutrophilia,	psoriasis, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,
used according to these assays are publicly available (e.g.,	through the ATCC) or may be isolated using techniques	disclosed herein or otherwise	known in the art. Natural	killer (NK) cells are large	granular lymphocytes that have	cytotoxic activity but do bind	antigen. NK cells show	antibody-independent killing	of tumor cells and also	recognize antibody bound on	target cells, via NK Fc	receptors, leading to cell-	mediated cytotoxicity.															
				1000																							-	

					meningitis, Lyme Disease, and
					allergy.
	HATBR65	786	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
39				by T cells and has strong	embodiment of the invention
\ 			-	effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
	- 17			has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
	1.55			myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
	-			regulated by cytokines, growth	and infection (e.g., as
			•	factors, and hormones are well	described below under
···				known in the art and may be	"Infectious Disease"). Highly
	_			used or routinely modified to	preferred indications include
-				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				including antibodies and	lupus erythematosis, multiple
				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and
				immunomodulation and	immunodeficiencies (e.g., as
				differentiation and modulate T	described below). Highly

			cell proliferation and function	nreferred indications also
		ad <del>1</del>	The state of the took for	include bootting a B cell-
			Exemplary assays that test for	include boosung a D cen-
			immunomodulatory proteins	mediated immune response
			evaluate the production of	and alternatively suppressing a
			cytokines, such as IL-6, and	B cell-mediated immune
			the stimulation and	response. Highly preferred
			upregulation of T cell	indications include
_			proliferation and functional	inflammation and
			activities. Such assays that	inflammatory
	<u></u>	-	may be used or routinely	disorders. Additional highly
			modified to test	preferred indications include
-			immunomodulatory and	asthma and allergy. Highly
			diffferentiation activity of	preferred indications include
			polypeptides of the invention	neoplastic diseases (e.g.,
-	-		(including antibodies and	myeloma, plasmacytoma,
			agonists or antagonists of the	leukemia, lymphoma,
			invention) include assays	melanoma, and/or as described
			disclosed in Miraglia et al., J	below under
	_		Biomolecular Screening 4:193-	"Hyperproliferative
			204(1999); Rowland et al.,	Disorders"). Highly preferred
			"Lymphocytes: a practical	indications include neoplasms
			approach" Chapter 6:138-160	and cancers, such as, myeloma,
			(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
			Immunol 158:2919-2925	lymphoma, melanoma, and
			(1997), the contents of each of	prostate, breast, lung, colon,
			which are herein incorporated	pancreatic, esophageal,
			by reference in its entirety.	stomach, brain, liver and
			Human dendritic cells that may	urinary cancer. Other preferred
-			be used according to these	indications include benign
			assays may be isolated using	dysproliferative disorders and
			techniques disclosed herein or	pre-neoplastic conditions, such

		outer wise allowin in the air.	as, ioi example, myperprasia,
		Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include
		suspension culture, which,	anemia, pancytopenia,
		when activated by antigen	leukopenia, thrombocytopenia,
		and/or cytokines, initiate and	Hodgkin's disease, acute
		upregulate T cell proliferation	lymphocytic anemia (ALL),
		and functional activities.	multiple myeloma, Burkitt's
		-	lymphoma, arthritis, AIDS,
		-	granulomatous disease,
			inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
	-		hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
			meningitis, and Lyme Disease.
			An additonal preferred
			indication is infection (e.g., an
			infectious disease as described
			below under "Infectious
			Disease").
HATBR65 987	Regulation of	Assays for the regulation of	A highly preferred
	transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
	Malic Enzyme in	are well-known in the art and	An additional highly preferred
	adipocytes	may be used or routinely	indication is a complication
		modified to assess the ability	associated with diabetes (e.g.,
		of polypeptides of the	diabetic retinopathy, diabetic
		invention (including antibodies	nephropathy, kidney disease

(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal	Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic	blockage), seizures, mental confusion, drowsiness,	hyperosmolar coma, cardiovascular disease (e.g.,	microvascular disease, hypertension, stroke, and other diseases and disorders as	described in the "Cardiovascular Disorders" section below), dyslipidemia,	endocrine disorders (as described in the "Endocrine Disorders" section below),	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection
and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis.	Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME promoter contains two direct	repeat (DR1)- like elements MEp and MEd identified as putative PPAR response	also responds to AP1 and other transcription factors.	used or routinely modified to test for regulation of	(in adipoocytes) by polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in: Streeper, R.S., et	al., Mol Endocrinol, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol	(1994); Barroso, I., et al., J Biol Chem, 274(25):17997- 8004 (1999); Iipenberg, A., et
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-	below, especially of the urinary tract and skin), carpal tunnel syndrome and ich is Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include d/or weight loss or alternatively, rated. highly preferred indications are	4IIE rat insulin resistance.  e. A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha for stimulating (e.g., increasing) TNF alpha increasing) TNF alpha indications include blood disorders (e.g., as described below under "Immune
al., J Biol Chem, 272(32):20108-20117 (1997); Berger, et al., Gene 66:1-10	(1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated.	may be used according to these assays includes the H4IIE rat liver hepatoma cell line.  Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved
		Activation of transcription through serum response element in immune cells (such as T-cells).
		HATCB92
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in growth. Exemplary assays	Activity", "Blood-Related
for transcription through the	Disorders", and/or
SRE that may be used or	"Cardiovascular Disorders"),
 routinely modified to test SRE	Highly preferred indications
activity of the polypeptides of	include autoimmune diseases
the invention (including	(e.g., rheumatoid arthritis,
antibodies and agonists or	systemic lupus erythematosis,
antagonists of the invention)	Crohn"s disease, multiple
include assays disclosed in	sclerosis and/or as described
Berger et al., Gene 66:1-10	below), immunodeficiencies
(1998); Cullen and Malm,	(e.g., as described below),
Methods in Enzymol 216:362-	boosting a T cell-mediated
368 (1992); Henthorn et al.,	immune response, and
Proc Natl Acad Sci USA	suppressing a T cell-mediated
85:6342-6346 (1988); and	immune response. Additional
Black et al., Virus Genes	highly preferred indications
12(2):105-117 (1997), the	include inflammation and
content of each of which are	inflammatory disorders, and
herein incorporated by	treating joint damage in
reference in its entirety. T	patients with rheumatoid
cells that may be used	arthritis. An additional highly
according to these assays are	preferred indication is sepsis.
publicly available (e.g.,	Highly preferred indications
through the ATCC).	include neoplastic diseases
Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
may be used according to these	and/or as described below
assays include the CTLL cell	under "Hyperproliferative
line, which is an IL-2	Disorders"). Additionally,
dependent suspension culture	highly preferred indications
of T cells with cytotoxic	include neoplasms and
activity.	cancers, such as, for example,

leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma). solid	tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and
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					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
41	HATCP77	686	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment
				role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune	of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferrred indication is
				disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly	the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),
				regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	and intection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described

			invention) to mediate	below) and
 •			immunomodulation and	immunodeficiencies (e.g., as
 	.,		differentiation and modulate T	described below). Highly
 			cell proliferation and function.	preferred indications also
 			Exemplary assays that test for	include boosting a B cell-
 		*	immunomodulatory proteins	mediated immune response
	_		evaluate the production of	and alternatively suppressing a
 -			cytokines, such as IL-6, and	B cell-mediated immune
	<del></del>		the stimulation and	response. Highly preferred
			upregulation of T cell	indications include
			proliferation and functional	inflammation and
 	<u></u>		activities. Such assays that	inflammatory
 _		_	may be used or routinely	disorders. Additional highly
	-P		modified to test	preferred indications include
	-		immunomodulatory and	asthma and allergy. Highly
			diffferentiation activity of	preferred indications include
 			polypeptides of the invention	neoplastic diseases (e.g.,
			(including antibodies and	myeloma, plasmacytoma,
 			agonists or antagonists of the	leukemia, lymphoma,
			invention) include assays	melanoma, and/or as described
 <del></del>			disclosed in Miraglia et al., J	below under
 т.			Biomolecular Screening 4:193-	"Hyperproliferative
			204(1999); Rowland et al.,	Disorders"). Highly preferred
<del></del>			"Lymphocytes: a practical	indications include neoplasms
 			approach" Chapter 6:138-160	and cancers, such as, myeloma,
 			(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
			Immunol 158:2919-2925	lymphoma, melanoma, and
•			(1997), the contents of each of	prostate, breast, lung, colon,
 	_		which are herein incorporated	pancreatic, esophageal,
	-		by reference in its entirety.	stomach, brain, liver and
			Human dendritic cells that may	urinary cancer. Other preferred

				he used according to these	indications include benign
				assavs may be isolated using	dysproliferative disorders and
				assays may or isolated using techniques disclosed herein or	re-neonlastic conditions such
				techniques disclosed herein of	pic incopiasite conditions, such
				otherwise known in the art.	as, ior example, nyperplasia,
		******		Human dendritic cells are	metaplasia, and/or dysplasia.
		···		antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HATEE46	066	Activation of	Kinase assay. JNK and p38	A highly preferred
42			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
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growth. An alternative highly preferred embodiment of the	invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for
apoptosis are well known in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	promote or inhibit cell	proliferation, activation, and	apoptosis. Exemplary assays	for JNK and p38 kinase	activity that may be used or	routinely modified to test JNK	and p38 kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.
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inhibiting (e.g., decreasing) the activation of and/or inactivating endothelial cells. A highly preferred embodiment of the invention	stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a	hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include	neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis
		_•	meopl descri "Hyp Disor the ca (e.g., heart aortic cardid regur regur dysfu
Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary endothelial cells	that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to,	angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	

and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications	endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as	well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that	stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.	Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer,
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na, ind	ors,							ghly	0		lon,		pt pt		l us	rs and	s, such	asia,	lasia.	ions	ase,		artery				ıs,	-	h as
si"s sarcor	lomus tum	, bacillary		othelioma,	<u>_</u> f	ricytoma,	la,	rcoma. H	cations als	rs such as,	st, lung, co	ophageal,	in, liver, a	r. Preferre	clude beni	ve disorde	c condition	le, hyperp	nd/or dysp	red indica	ırterial dise	osclerosis	, coronary	mmatory	Reynaud"s	eynaud"s	ı, aneurysn	enous and	sorders suc
such as, Kaposi"s sarcoma, hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as
suc	cav	tela	ang	her	ang	hae	lyn	lyn	pre	inc	pro	par	sto	uri	ind	dys	pre	as,	me	Hil	als	ns	hy	dis	va	dis	qd	res	lyr
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thrombonhlebitic	unomportes,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred
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indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,	inflammatory bowel disease	and Crohn's disease), and pain	management.	Preferred embodiments of the	invention include using	y polypeptides of the invention		antagonists thereof) in
																										Assays for measuring	expression of ICAM-1 are	well-known in the art and may	be used or routinely modified	to assess the ability of
				. 1.					-																	Production of	ICAM-1			
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detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Inflammation, Vascular Jy Sestenosis, and Stroke It It Its Ays Ays Ays Ays Ays Ays Ays Ays Ays	Highly preferred indications include asthma, allergy, on, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
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_	polypeptides of the invention	and hematonoietic disorders	
	(including antibodies and	(e.g., as described below under	
	agonists or antagonists of the	"Immune Activity", and	
	invention) to promote or	"Blood-Related Disorders"),	
	inhibit cell proliferation,	autoimmune diseases (e.g.,	
	activation, and apoptosis.	rheumatoid arthritis, systemic	
	Exemplary assays for JNK	lupus erythematosis, Crohn"s	
	kinase activity that may be	disease, multiple sclerosis	
	used or routinely modified to	and/or as described below),	
	test JNK kinase-induced	immunodeficiencies (e.g., as	
	activity of polypeptides of the	described below). Highly	
	invention (including antibodies	s preferred indications also	
	and agonists or antagonists of	include boosting or inhibiting	
	the invention) include the	immune cell proliferation.	
	assays disclosed in Forrer et	Preferred indications include	
	al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,	
	1110 (1998); Gupta et al., Exp		
	Cell Res 247(2): 495-504	described below under	
	(1999); Kyriakis JM, Biochem	"Hyperproliferative	
	Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred	
	Chang and Karin, Nature	indications include boosting an	
	410(6824):37-40 (2001); and	eosinophil-mediated immune	
	Cobb MH, Prog Biophys Mol	response, and suppressing an	
	Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune	
	the contents of each of which	response.	
	are herein incorporated by		
	reference in its entirety.		
	Exemplary cells that may be		
	used according to these assays		
	include eosinophils.		
	Eosinophils are important in		

the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction.  Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38	mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor	signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999

y and, vo oids in ociated NN- lure of JUN N- regy (3 Pt ontents rein ce in its	ase trightly preferred indications include asthma, allergy, eration, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under of the "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis fied to and/or as described below),
Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis.  Exemplary assays for JNK kinase activity that may be used or routinely modified to
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
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(1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be
include eosinophils.  Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late

invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000);	"Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase

HBCPB32 994 Activation of transcription through the include blood disorders (e.g., through NIPAT response element in earlied some cells, or s					phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	
transcription through NFAT response element in immune cells (such as natural killer may be used or routinely cells).  of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT- response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays		HBCPB32	994	Activation of	Assays for the activation of	Highly preferred indications
are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	46	-		transcription through NFAT	transcription inrough me Nuclear Factor of Activated T	as described below under
may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT- response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays				response element in	cells (NFAT) response element	"Immune Activity", "Blood- Related Disorders" and/or
modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays				as natural killer	may be used or routinely	"Cardiovascular Disorders").
				cells).	modified to assess the ability	Highly preferred indications
				`	of polypeptides of the	include autoimmune diseases
				<del></del>	invention (including antibodies	(e.g., rheumatoid arthritis,
rs and enes ions.  of tion the					and agonists or antagonists of	systemic lupus erythematosis,
					the invention) to regulate	multiple sclerosis and/or as
					NFAT transcription factors and	described below),
dulatory functions. assays for n through the onse element that d or routinely test NFAT-ement activity of so of the invention antibodies and antagonists of the include assays				-	modulate expression of genes	immunodeficiencies (e.g., as
					involved in	described below), boosting a T
that  of  tition  f the					immunomodulatory functions.	cell-mediated immune
that of of the o					Exemplary assays for	response, and suppressing a T
t that  y y of y of that of					transcription through the	cell-mediated immune
y of antion id					NFAT response element that	response. Additional highly
y of nation and soft the					may be used or routinely	preferred indications include
<b>T</b> • • • • • • • • • • • • • • • • • • •					modified to test NFAT-	inflammation and
<b>5</b> 1)					response element activity of	inflammatory disorders. An
					polypeptides of the invention	additional highly preferred
		***************************************			(including antibodies and	indication is infection (e.g., an
					agonists or antagonists of the	infectious disease as described
					invention) include assays	below under "Infectious

Disease"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms	and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign	itsorders and nditions, such hyperplasia, or dysplasia. ions also bancytopenia,	bocytopenia, , acute iia (ALL), nultiple 's lymphoma, anulomatous tory bowel utropenia, asis,
	and cancers, such as, for example, leukemia, lymphoma and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.  Preferred indications also include anemia, pancytopenia, last an example.	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which	are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.
			,

reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia,
	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
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routinely modified to test	lymphoma, melanoma,
GATA3-resnonse element	nrostate breast lung colon
activity of polypeptides of the	
invention (including antibodies	es stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	
disclosed in Berger et al., Gene	ne "Hyperproliferative
 66:1-10 (1998); Cullen and	
Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	n dysproliferative disorders and
et al., Proc Natl Acad Sci USA	
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	
   Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	
Henderson et al., Mol Cell Biol	ol   (ALL), plasmacytomas,
 14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
contents of each of which are	
herein incorporated by	granulomatous disease,
reference in its entirety. Mast	inflammatory bowel disease,
cells that may be used	sepsis, neutropenia,
according to these assays are	neutrophilia, psoriasis,
publicly available (e.g.,	suppression of immune
through the ATCC).	reactions to transplanted
Exemplary human mast cells	organs and tissues, hemophilia,
that may be used according to	hypercoagulation, diabetes
 these assays include the HMC-	
1 cell line, which is an	meningitis, and Lyme Disease.

				immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	
47	нвс0132	962	Activation of transcription	This reporter assay measures activation of the NFAT	Highly preferred indications include allergy, asthma, and
			response element in immune cells (such	human mast cell line. Activation of NFAT in mast	indications include infection  (e.g., an infectious disease as
			as mast cells).	cells has been linked to cytokine and chemokine	described below under "Infectious Disease"), and
				production. Assays for the activation of transcription	inflammation and inflammatory disorders.
				through the Nuclear Factor of Activated T cells (NFAT)	Preferred indications also include blood disorders (e.g.,
				response element are well- known in the art and may be	as described below under "Immune Activity", "Blood-
	, ,			used or routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders").
				polypeptides of the invention (including antibodies and	Preferred indications include
			PLACE	agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT transcription factors and	lupus erythematosis, multiple sclerosis and/or as described
			, , ,	modulate expression of genes involved in	below) and imminodeficiencies (e. σ. as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
				transcription inrough the	diseases (e.g., leukemia,

lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary tract cancers and/or as described below under "Hyperproliferative"	Disorders"). Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease, acute lymphocytic anemia	(ALL), plasmacytomas, multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS, granulomatous disease,	sepsis, neutropenia,	neutrophilia, psoriasis, suppression of immune	reactions to transplanted organs and tissues, hemophilia,	hypercoagulation, diabetes	meningitis, and Lyme Disease.
NFAT response element that may be used or routinely modified to test NFAT-response element activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali	et al., J Immunol 165(12):7215-7223 (2000);	Hutchinson and McCloskey, J Biol Chem 270(27):16333-	16338 (1995), and Turner et al., J Exp Med 188:527-537	which are herein incorporated	by reference in its entirety.  Mast cells that may be used	according to these assays are publicly available (e.g.,	through the ATCC).	that may be used according to
						· · · · · · · · · · · · · · · · · · ·						

				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
Name .			-	blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HBGNU56	966	Activation of	Kinase assay. Kinase assays,	A highly preferred
48			Hepatocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating hepatocyte cell
				proliferation or differentiation	proliferation. An alternative
1				are well known in the art and	highly preferred embodiment
_			-	may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
	-			of polypeptides of the	hepatocyte cell proliferation.
				invention (including antibodies	A highly preferred
				and agonists or antagonists of	embodiment of the invention
				the invention) to promote or	includes a method for
			-	inhibit cell proliferation,	stimulating hepatocyte cell
				activation, and differentiation.	differentiation. An alternative
				Exemplary assays for ERK	highly preferred embodiment
	-			kinase activity that may be	of the invention includes a
				used or routinely modified to	method for inhibiting
				test ERK kinase-induced	hepatocyte cell differentiation.
				activity of polypeptides of the	A highly preferred
				invention (including antibodies	embodiment of the invention
				and agonists or antagonists of	includes a method for
				the invention) include the	activating hepatocyte cells. An
				assays disclosed in Forrer et	alternative highly preferred

al., Biot Chem 3/9(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Rat liver hepatoma cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary rat liver hepatoma cells that may be used according to these assays include H4lle cells, which are known to respond to glucocorticoids, insulin, or cAMP derivatives.

indication is a complication associated with diabetes (e.g.,	diabetic retinopathy, diabetic nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Kenal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),
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neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and	disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture).	An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are	highly preferred indications are complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hepatitis, jaundice, gallstones, cirrhosis of the liver, degenerative or

necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and chlolesterol metabolism. Additional highly preferred indications include neoplasms and cancers, such as, hepatocarcinomas, other liver cancers, and colon and pancreatic cancer. Preferred indications also include prostate, breast, lung, esophageal, stomach, brain, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	ays A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNo Highly preferred
	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation: and
	Production of IFNgamma using a T cells
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	HBHAD12
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indications include blood	tory disorders (e.g., as described			Disorders", and/or	"Cardiovascular Disorders"),				chronic granulomatosus		osteoporosis, and/or as	he described below under	"Infectious Disease"). Highly		autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	tys   below), immunodeficiency		solution is a self-mediated	immune response, and		immune response. Additional		include inflammation and	inflammatory disorders.	y of   Additional preferred	on indications include idiopathic	pulmonary fibrosis. Highly
increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and
	M-s								,																					
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preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under	"Hyperproliterative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for	example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis. AIDS. oranulomatous	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al.,	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol	15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the	contents of each of which are herein incorporated by reference in its entirety.	Human T cells that may be used according to these assays may be isolated using	techniques disclosed herein or otherwise known in the art. Human T cells are primary	human lymphocytes that mature in the thymus and express a T Cell receptor and	cells mediate humoral or cellmediated immunity and may be preactivated to enhance
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				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
_					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HBHMA23	866	Production of TNF	TNFa FMAT. Assays for	A highly preferred
50			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
		1000		and other cell types that exert a	alternative highly preferred
			-	wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
-				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications
				the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
				antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
				and the induction or inhibition	(e.g., as described below),

boosting a T cell-mediated immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,
of an inflammatory or cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are
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and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis	***************************************	neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include boosting an eosinophil-mediated immune response, and suppressing an eosinophil-mediated immune response.
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis.  Exemplary assays for JNK kinase activity that may be	used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils.

the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999
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Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC
	Inhibition of squalene synthetase gene transcription.
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activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders	(e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic	diseases (e.g., lipomas, liposarcomas, and/or as described below under "Hyperproliferative"	<del>-</del>	congestive heart failure, blood vessel blockage, heart disease,	stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disordars".	and/or "Blood-Related Disorders"), immune disorders	(e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Neural Activity	and Neurological Diseases"), and infection (e.g., as described below under "Infectious Disease").
Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang	and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999);	the contents of each of which are herein incorporated by reference in its entirety.  Mouse adinocyte cells that	may be used according to these assays are publicly available	Exemplary mouse adipocyte cells that may be used	according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse	preaupocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed	undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation	conditions known in the art.

			disease, dyslipidemia,
			gallstones, osteoartmrits, degenerative arthritis, eating
			disorders, fibrosis, cachexia,
			and kidney diseases or disorders. Preferred
			indications include neoplasms
			and cancer, such as,
			lymphoma, leukemia and
			breast, colon, and kidney
			cancer. Additional preferred
			indications include melanoma,
			prostate, lung, pancreatic,
			esophageal, stomach, brain,
			liver, and urinary cancer.
			Highly preferred indications
			include lipomas and
			liposarcomas. Other preferred
			indications include benign
			dysproliferative disorders and
			pre-neoplastic conditions, such
			as, for example, hyperplasia,
			metaplasia, and/or dysplasia.
 1001	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
		by T cells and has strong	embodiment of the invention
		effects on B cells. IL-6	includes a method for
		participates in IL-4 induced	stimulating (e.g., increasing)
		IgE production and increases	IL-6 production. An alternative
		IgA production (IgA plays a	highly preferred embodiment
		role in mucosal immunity).	of the invention includes a
		IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,

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	reducing) IL-6 production. A	highly preferred indication is	the stimulation or enhancement	of mucosal immunity. Highly	preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	1: 2: 11: 1 1: 11: 1 1: 11: 11: 11: 11:
	Deregulated expression of IL-6   reducing) IL-6 production. A	has been linked to autoimmune	disease, plasmacytomas,	myelomas, and chronic	hyperproliferative diseases.	Assays for immunomodulatory	and differentiation factor	proteins produced by a large	variety of cells where the	expression level is strongly	regulated by cytokines, growth	factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	
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inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the
	Production of IL-6
	HBJIY92
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	expression level is strongly	"Cardiovascular Disorders")
	regulated by cytokines, growth	and infection (e.g. as
	factors, and hormones are well	described below under
	known in the art and may be	"Infectious Disease"). Highly
	used or routinely modified to	preferred indications include
	assess the ability of	autoimmune diseases (e.g.,
	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders. Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
-	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative

		2	204(1999); Rowland et al.,	Disorders"). Highly preferred
		<u> </u>	"Lymphocytes: a practical	indications include neoplasms
		<u> </u>	approach" Chapter 6:138-160	and cancers, such as, myeloma,
		<u> </u>	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
-		<u>п</u>	Immunol 158:2919-2925	Jymphoma, melanoma, and
		<u> </u>	(1997), the contents of each of	prostate, breast, lung, colon,
		8	which are herein incorporated	pancreatic, esophageal,
		<u> </u>	by reference in its entirety.	stomach, brain, liver and
		<u> </u>	Human dendritic cells that may	urinary cancer. Other preferred
	1. 2.1.	<u> </u>	be used according to these	indications include benign
		8	assays may be isolated using	dysproliferative disorders and
		te	techniques disclosed herein or	pre-neoplastic conditions, such
		0	otherwise known in the art.	as, for example, hyperplasia,
		<u> </u>	Human dendritic cells are	metaplasia, and/or dysplasia.
		<u>a</u>	antigen presenting cells in	Preferred indications include
		NS ST	suspension culture, which,	anemia, pancytopenia,
			when activated by antigen	leukopenia, thrombocytopenia,
		<u>a</u>	and/or cytokines, initiate and	Hodgkin's disease, acute
		n n	upregulate T cell proliferation	lymphocytic anemia (ALL),
	_		and functional activities.	multiple myeloma, Burkitt's
				lymphoma, arthritis, AIDS,
		**		granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
		•		organs and tissues,
		-		hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.

,					An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
45	HBJIY92	1002	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing)  TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)  TNF alpha production.  Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below),
				of an inflammatory or cytotoxic response. Such	boosting a 1 cell-mediated immune response, and

assays that may be used or	suppressing a T cell-mediated
routinely modified to test	immune response. Additional
Immunomodulatory activity of	highly preferred indications
furthermore of the invention (including antibodies and	inflammatory disorders and
agonists or antagonists of the	treating joint damage in
invention) include assays	patients with rheumatoid
disclosed in Miraglia et al., J	arthritis. An additional highly
Biomolecular Screening 4:193-	preferred indication is sepsis.
204(1999); Rowland et al.,	Highly preferred indications
"Lymphocytes: a practical	include neoplastic diseases
approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
(2000); Verhasselt et al., Eur J	and/or as described below
Immunol 28(11):3886-3890	under "Hyperproliferative
(1198); Dahlen et al., J	Disorders"). Additionally,
Immunol 160(7):3585-3593	highly preferred indications
(1998); Verhasselt et al., J	include neoplasms and
Immunol 158:2919-2925	cancers, such as, leukemia,
(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
(1999), the contents of each of	tumors, and prostate, breast,
which are herein incorporated	lung, colon, pancreatic,
by reference in its entirety.	esophageal, stomach, brain,
Human dendritic cells that may	liver and urinary cancer. Other
be used according to these	preferred indications include
assays may be isolated using	benign dysproliferative
techniques disclosed herein or	disorders and pre-neoplastic
otherwise known in the art.	conditions, such as, for
Human dendritic cells are	example, hyperplasia,
antigen presenting cells in	metaplasia, and/or dysplasia.
suspension culture, which,	Preferred indications include

				when activated by antigen	anemia, pancytopenia,
				and/or cytokines, initiate and	leukopenia, thrombocytopenia,
				upregulate T cell proliferation	Hodgkin's disease, acute
				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
•					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
		-			cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
				,	disease as described below
	TIGOT TIGHT				under "Infectious Disease").
22	HBJLCUI	1003	Activation of	Kinase assay. Kinase assays,	A highly preferred
23			Adipocyte PI3	for example an GSK-3 assays,	embodiment of the invention
			Kinase Signalling	for PI3 kinase signal	includes a method for
			Pathway	transduction that regulate	increasing adipocyte survival
				glucose metabolism and cell	An alternative highly preferred
				survival are well-known in the	embodiment of the invention
				art and may be used or	includes a method for
				routinely modified to assess	decreasing adipocyte survival.
				the ability of polypeptides of	A preferred embodiment of the

	the invention (including	invention includes a method
	antibodies and agonists or	Ior stimulating adipocyte
	antagonists of the invention) to	proliferation. An alternative
	promote or inhibit glucose	highly preferred embodiment
	metabolism and cell survival.	of the invention includes a
	Exemplary assays for PI3	method for inhibiting
	kinase activity that may be	adipocyte proliferation. A
 	used or routinely modified to	preferred embodiment of the
	test PI3 kinase-induced activity	invention includes a method
	of polypeptides of the	for stimulating adipocyte
	invention (including antibodies	differentiation. An alternative
	and agonists or antagonists of	highly preferred embodiment
	the invention) include assays	of the invention includes a
	disclosed in Forrer et al., Biol	method for inhibiting
 	Chem 379(8-9):1101-1110	adipocyte differentiation.
	(1998); Nikoulina et al.,	Highly preferred indications
	Diabetes 49(2):263-271	include endocrine disorders
	(2000); and Schreyer et al.,	(e.g., as described below under
	Diabetes 48(8):1662-1666	"Endocrine Disorders").
	(1999), the contents of each of	Preferred indications include
	which are herein incorporated	neoplastic diseases (e.g.,
	by reference in its entirety.	lipomas, liposarcomas, and/or
	Mouse adipocyte cells that	as described below under
	may be used according to these	"Hyperproliferative
	assays are publicly available	Disorders"), blood disorders
	(e.g., through the ATCC).	(e.g., hypertension, congestive
	Exemplary mouse adipocyte	heart failure, blood vessel
	cells that may be used	blockage, heart disease, stroke,
	according to these assays	impotence and/or as described
	include 3T3-L1 cells. 3T3-L1	below under "Immune
	is an adherent mouse	Activity", "Cardiovascular

confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal	tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively,

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weight gain. Additional highly preferred indications are	complications associated with insulin resistance.	hly preferred	indications are disorders of the	al systems	pathies,	muscular dystrophy, and/or as		hly preferred	lude,	coronary artery	idemia,	soarthritis,	rthritis, eating	sis, cachexia,	eases or	disorders. Highly preferred	indications include neoplasms	ch as, lipoma,	/mphoma,	reast, colon,	and kidney cancer. Additional	d indications	oma, prostate,	lung, pancreatic, esophageal,	n, liver, and	urinary cancer. Other preferred	lude benign	dysproliferative disorders and
weight gain. highly preferre	insulin resistance.	Additional highly preferred	indications are	musculoskeletal systems	including myopathies,	muscular dystre	described nerein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. H	indications incl	and cancer, such as, lipoma,	liposarcoma, lymphoma,	leukemia and breast, colon,	and kidney can	highly preferred indications	include melanoma, prostate,	lung, pancreat	stomach, brain, liver, and	urinary cancer.	indications include benign	dysproliferative
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					pre-neoplastic conditions, such as, for example, hyperplasia,
	HBJLC01	1003	Activation of	Assays for the activation of	A highly preferred indication
55		,	transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
		TAIT TO	response element	well-known in the art and may	Additional highly preferred
2			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
				transcription through the	nonketotic hyperglycemic-

hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	Additional highly preferred	indications are complications	associated with insulin	resistance.				
cAMP response element that may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem	273:917-923 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse
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				preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
	IID II CO1	1000	J; 7; 7 - V	Coliditions Knowil III the art.	n. f 1 : . 1:
1	HBJCC01	1003	Activation of	Assays for the activation of	Preferred indications
55			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are known in	(e.g., as described below under
			response element in	the art and may be used or	"Hyperproliferative
			immune cells (such	routinely modified to assess	Disorders"), blood disorders
			as T-cells).	the ability of polypeptides of	(e.g., as described below under
				the invention (including	"Immune Activity",
				antibodies and agonists or	"Cardiovascular Disorders",
				antagonists of the invention) to	and/or "Blood-Related
				modulate growth and other cell	Disorders"), and infection
				functions. Exemplary assays	(e.g., an infectious disease as
	·			for transcription through the	described below under
				AP1 response element that	"Infectious Disease"). Highly
				may be used or routinely	preferred indications include
				modified to test AP1-response	autoimmune diseases (e.g.,
				element activity of	rheumatoid arthritis, systemic
				polypeptides of the invention	lupus erythematosis, multiple
				(including antibodies and	sclerosis and/or as described
	-			agonists or antagonists of the	below) and
				invention) include assays	immunodeficiencies (e.g., as
				disclosed in Berger et al., Gene	described below). Additional
				66:1-10 (1988); Cullen and	highly preferred indications
	,			Malm, Methods in Enzymol	include inflammation and

of immune reactions to transplanted organs and tissues, endocarditis, meninoitis, and I vme Disease	oduced		IgA production (IgA plays a highly preferred embodiment role in micosal imminity)	ells.		disease, plasmacytomas, the stimulation or enhancement			Assays for immunomodulatory   blood disorders (e.g., as	tiation factor described below under	.ge			regulated by cytokines, growth   and infection (e.g., as	factors, and hormones are well   described below under	known in the art and may be "Infectious Disease"). Highly	used or routinely modified to preferred indications include	ility of autoimmune diseases (e.g.,	polypeptides of the invention   rheumatoid arthritis, systemic		agonists or antagonists of the sclerosis and/or as described	
	Production of IL-6 IL-6 FMAT. IL-6 is proby T cells and has stron effects on B cells II-6	participates i IgE producti	IgA producti	IL-6 induces	Deregulated	ilas been miked to autom disease, plasmacytomas,	myelomas, and chronic	hyperprolifer	Assays for in	and differentiation factor	proteins prod	variety of cel	expression le	regulated by	factors, and h	known in the	used or routir	assess the ability of	polypeptides	(including antibodies and	agonists or an	-to:Louis of (moitmonni)
	1003																					
	HBJLC01																					-
	55							-						_								

				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
		_		Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
-				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
		~		upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
			-		inflammatory bowel disease,
					sepsis, neutropenia,
			-		neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
-					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
	TIPIT CO.				Disease").
2.2	HBJLC01	1003	Activation of	Assays for the activation of	Highly preferred indications
CC			transcription	transcription through the	include allergy, asthma, and
			through STAT6	Signal Transducers and	rhinitis. Additional highly
			response element in	Activators of Transcription	preferred indications include
			immune cells (such	(STAT6) response element in	infection (e.g., an infectious

disease as described below under "Infectious Disease"),	and inflammation and	inflammatory disorders.	Preferred indications also	include hematopoietic and	immunological disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma, and/or	as described below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other
immune cells (such as in the human HMC-1 mast cell line)	are well-known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to regulate	STAT6 transcription factors	and modulate the expression of	multiple genes. Exemplary	assays for transcription	through the STAT6 response	element that may be used or	routinely modified to test	STAT6 response element	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988);	Sherman, Immunol Rev	179:48-56 (2001); Malaviya	and Uckun, J Immunol
as mast cells).																												-	
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ļ				168:421-426 (2002); Masuda	preferred indications include
				et al., J Biol Chem	benign dysproliferative
				275(38):29331-29337 (2000);	disorders and pre-neoplastic
				and Masuda et al., J Biol Chem	conditions, such as, for
				276:26107-26113 (2001), the	example, hyperplasia,
			-	contents of each of which are	metaplasia, and/or dysplasia.
<del></del>	, <u>, , , , , , , , , , , , , , , , , , </u>			herein incorporated by	Preferred indications include
				reference in its entirety. Mast	hematopoietic and
				cells that may be used	immunological disorders such
				according to these assays are	as arthritis, AIDS,
				publicly available (e.g.,	granulomatous disease,
	-			through the ATCC).	inflammatory bowel disease,
				Exemplary human mast cells	sepsis, neutropenia,
				that may be used according to	neutrophilia, psoriasis,
				these assays include the HMC-	suppression of immune
				1 cell line, which is an	reactions to transplanted
			•	immature human mast cell line	organs and tissues, hemophilia,
				established from the peripheral	hypercoagulation, diabetes
				blood of a patient with mast	mellitus, endocarditis,
	13.			cell leukemia, and exhibits	meningitis, and Lyme Disease.
				many characteristics of	
				immature mast cells.	
!	HBJLC01	1003	Production of	RANTES FMAT. Assays for	
55			RANTES in	immunomodulatory proteins	
			endothelial cells	that induce chemotaxis of T	
			such as human	cells, monocytes, and	
			umbilical vein	eosinophils are well known in	
	-		endothelial cells	the art and may be used or	
			(HUVEC))	routinely modified to assess	
				the ability of polypeptides of	
				the invention (including	

antibodies and aconists or	antagonists of the invention) to	mediate immunomodulation,	induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated
								-																				4.		
									***																					
									_																					

ety.  lay be assays e.g.,  cells ling to man ial cells line nd are nd are nd are one, one,	n of Preferred indications e AP1 include neoplastic diseases hown in (e.g., as described below under sess) les of (e.g., as described below under "Immune Activity", or "Cardiovascular Disorders", tion) to and/or "Blood-Related her cell Disorders", and infection e.g., an infectious disease as described below under (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications includes
by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular tone, and immune cell extravasation.	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that
	transcription through AP1 response element in immune cells (such as T-cells).
	HBJLF01

modified to test AP1-response	autoimmune diseases (e.g.,
element activity of	rheumatoid arthritis, systemic
polypeptides of the invention	lupus erythematosis, multiple
(including antibodies and	sclerosis and/or as described
agonists or antagonists of the	below) and
 invention) include assays	immunodeficiencies (e.g., as
disclosed in Berger et al., Gene	described below). Additional
66:1-10 (1988); Cullen and	highly preferred indications
 Malm, Methods in Enzymol	include inflammation and
216:362-368 (1992); Henthorn	inflammatory disorders.
et al., Proc Natl Acad Sci USA	Highly preferred indications
85:6342-6346 (1988);	also include neoplastic
Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
272(49):30806-30811 (1997);	lymphoma, and/or as described
Chang et al., Mol Cell Biol	below under
18(9):4986-4993 (1998); and	"Hyperproliferative
Fraser et al., Eur J Immunol	Disorders"). Highly preferred
 29(3):838-844 (1999), the	indications include neoplasms
contents of each of which are	and cancers, such as, leukemia,
 herein incorporated by	lymphoma, prostate, breast,
reference in its entirety. T	lung, colon, pancreatic,
cells that may be used	esophageal, stomach, brain,
according to these assays are	liver, and urinary cancer. Other
publicly available (e.g.,	preferred indications include
 through the ATCC).	benign dysproliferative
Exemplary mouse T cells that	disorders and pre-neoplastic
may be used according to these	conditions, such as, for
 assays include the CTLL cell	example, hyperplasia,
line, which is an IL-2	metaplasia, and/or dysplasia.
dependent suspension-culture	Preferred indications include
cell line with cytotoxic	arthritis, asthma, AIDS,

				activity.	allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
26	HBJLF01	1004	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred inflammation and inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred

indications include neoplasms and cancers such as, for example, leukemia, lymphoma, melanoma, renal cell carcinoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as
vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	Activation of transcription through STAT6 response element in immune cells (such as T-cells).
	1005
	HBJLH40
	57

	agonists or antagonists of the	ne described below under
	invention) to regulate STAT6	F6 "Immune Activity", "Blood-
	transcription factors and	Related Disorders", and/or
	modulate the expression of	
	multiple genes. Exemplary	
-	assays for transcription	autoimmune diseases (e.g.,
	through the STAT6 response	4)
	element that may be used or	
	routinely modified to test	
	STAT6 response element	
	activity of the polypeptides of	of   immunodeficiencies (e.g., as
	the invention (including	described below).
	antibodies and agonists or	Preferred indications include
	antagonists of the invention)	neoplastic diseases (e.g.,
	include assays disclosed in	leukemia, lymphoma,
	Berger et al., Gene 66:1-10	melanoma, and/or as described
	(1998); Cullen and Malm,	below under
	Methods in Enzymol 216:362-	62- Whyperproliferative
	368 (1992); Henthorn et al.,	
	Proc Natl Acad Sci USA	indications include neoplasms
	85:6342-6346 (1988); Georas	
	et al., Blood 92(12):4529-4538	
	(1998); Moffatt et al.,	
	Transplantation 69(7):1521-	
	1523 (2000); Curiel et al., Eur	ur stomach, brain, liver and
	J Immunol 27(8):1982-1987	urinary cancer. Other preferred
	(1997); and Masuda et al., J	indications include benign
	Biol Chem 275(38):29331-	dysproliferative disorders and
	29337 (2000), the contents of	of pre-neoplastic conditions, such
	each of which are herein	as, for example, hyperplasia,
	incorporated by reference in its	its metaplasia, and/or dysplasia.

entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.  HBJNC59 1006 Activation of T- Kinase assay. JNK and p38 Cell p38 or JNK kinase assays for signal Signaling Pathway. transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including

		antibodies and agonists or	Disorders"), and infection
		antagonists of the invention) to	(e.g., an infectious disease as
		promote or inhibit immune cell	described below under
		(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
		activation, and apoptosis.	preferred indications include
		Exemplary assays for JNK and	autoimmune diseases (e.g.,
		p38 kinase activity that may be	rheumatoid arthritis, systemic
-		used or routinely modified to	lupus erythematosis, multiple
		test JNK and p38 kinase-	sclerosis and/or as described
		induced activity of	below) and
		polypeptides of the invention	immunodeficiencies (e.g., as
		(including antibodies and	described below). Additional
		agonists or antagonists of the	highly preferred indications
		invention) include the assays	include inflammation and
	-	disclosed in Forrer et al., Biol	inflammatory disorders.
		Chem 379(8-9):1101-1110	Highly preferred indications
		(1998); Gupta et al., Exp Cell	also include neoplastic
		Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
		Kyriakis JM, Biochem Soc	lymphoma, and/or as described
-		Symp 64:29-48 (1999); Chang	below under
		and Karin, Nature	"Hyperproliferative
	NO SAL	410(6824):37-40 (2001); and	Disorders"). Highly preferred
		Cobb MH, Prog Biophys Mol	indications include neoplasms
		Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
~		the contents of each of which	lymphoma, prostate, breast,
,		are herein incorporated by	lung, colon, pancreatic,
		reference in its entirety. T	esophageal, stomach, brain,
		cells that may be used	liver, and urinary cancer. Other
		according to these assays are	preferred indications include
		publicly available (e.g.,	benign dysproliferative
		through the ATCC).	disorders and pre-neoplastic

				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt"s lymphoma,
					granulomatous disease,
	-				inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HBMCI50	1007	Production of IL-8	Assay that measures the	Highly preferred indications
59		·	by immune cells	production of the chemokine	include eosinophilia, asthma,
			(such as the human	interleukin-8 (IL-8) from	allergy, hypersensitivity
			EOL-1 eosinophil	immune cells (such as the	reactions, inflammation, and
			cells)	EOL-1 human eosinophil cell	inflammatory disorders.
				line) are well known in the art	Additional highly preferred
				(for example, measurement of	indications include immune
				IL-8 production by FMAT)	and hematopoietic disorders
				and may be used or routinely	(e.g., as described below under
				modified to assess the ability	"Immune Activity", and
				of polypeptides of the	"Blood-Related Disorders"),
				invention (including antibodies	autoimmune diseases (e.g.,
				and agonists or antagonists of	rheumatoid arthritis, systemic

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lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting or inhibiting immune cell proliferation. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include boosting an eosinophil-mediated immune response, and suppressing an eosinophil-mediated immune response.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under
the invention) to promote or inhibit. Eosinophils are a type of immune cell important in allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. IL8 is a strong immunomodulator and may have a potential proinflammatory role in immunological diseases and disorders (such as allergy and asthma).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
	1007
	HBMCI50
	59

routinely modified to assess	"Immine Activity" "Blood-
the ability of polypeptides of	Related Disorders", and/or
the invention (including	"Cardiovascular Disorders").
antibodies and agonists or	Preferred indications include
antagonists of the invention) to	
regulate GATA3 transcription	
 factors and modulate	lupus erythematosis, multiple
expression of mast cell genes	sclerosis and/or as described
important for immune response	
development. Exemplary	immunodeficiencies (e.g., as
assays for transcription	described below). Preferred
 through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
 routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	-
invention (including antibodies	s stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	described below under
disclosed in Berger et al., Gene	e ''Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
 85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	
Quant Biol 64:563-571 (1999);	
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	
Cell 89(4):587-596 (1997); and	

				Henderson et al., Mol Cell Biol (ALL), plasmacytomas,	(ALL), plasmacytomas.
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
			,	through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	,
				established from the peripheral	
74				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HBMCI50	1007	Activation of	This reporter assay measures	Highly preferred indications
59			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
,			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
-			as mast cells).	cells has been linked to	described below under
	`			cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
		•		Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under

	known in the art and may he	"Immine Activity" "Blood
	of position in continuous	Deleted Discussion, 2000
	or nationalist incontract to	Kelaled Disorders, and/or
	assess the ability of	"Cardiovascular Disorders").
	polypeptides of the invention	Preferred indications include
	(including antibodies and	autoimmune diseases (e.g.,
	agonists or antagonists of the	rheumatoid arthritis, systemic
	invention) to regulate NFAT	lupus erythematosis, multiple
	transcription factors and	sclerosis and/or as described
	modulate expression of genes	below) and
	involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
-	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia

				Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		•		Biol Chem 2/0(2/):16333- 16338 (1995) and Turner et	multiple myeloma, Burkitt's
				al J Exp Med 188:527-537	granulomatous disease.
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HBMCI50	1007	Production of	Endothelial cells, which are	Highly preferred indications
59			ICAM in	cells that line blood vessels,	include inflammation (acute
	-		endothelial cells	and are involved in functions	and chronic), restnosis,
			(such as human	that include, but are not limited	atherosclerosis, asthma and
			umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
· · · · · ·			endothelial cells	permeability, vascular tone,	indications include
			(HUVEC))	and immune cell extravasation.	inflammation and
				Exemplary endothelial cells	inflammatory disorders,
				that may be used in ICAM	immunological disorders,
				production assays include	neoplastic disorders (e.g.

	nq	human umbilical vein	cancer/tumorigenesis), and
	en	endothelial cells (HUVEC),	cardiovascular disorders (such
	an	and are available from	as described below under
	000	commercial sources. The	"Immune Activity", "Blood-
	ex)	expression of ICAM (CD54),a	Related Disorders",
	int	intergral membrane protein,	"Hyperproliferative Disorders"
	cal	can be upregulated by	and/or "Cardiovascular
	cyl	cytokines or other factors, and	Disorders"). Highly preferred
		ICAM expression is important	indications include neoplasms
	ii	in mediating immune and	and cancers such as, for
	enc	endothelial cell interactions	example, leukemia, lymphoma,
	lea	leading to immune and	melanoma, renal cell
	<u>fui</u>	inflammatory responses.	carcinoma, and prostate,
	As	Assays for measuring	breast, lung, colon, pancreatic,
	exi	expression of ICAM-1 are	esophageal, stomach, brain,
-	We	well-known in the art and may	liver and urinary cancer. Other
	l pe	be used or routinely modified	preferred indications include
	to	to assess the ability of	benign dysproliferative
	od	polypeptides of the invention	disorders and pre-neoplastic
		(including antibodies and	conditions, such as, for
	age a	agonists or antagonists of the	example, hyperplasia,
	ni	invention) to regulate ICAM-1	metaplasia, and/or dysplasia.
	ex	expression. Exemplary assays	
	the	that may be used or routinely	
	om mc	modified to measure ICAM-1	
	ex	expression include assays	
	dis	disclosed in: Rolfe BE, et al.,	
	At	Atherosclerosis, 149(1):99-110	
	(20	(2000); Panettieri RA Jr, et al.,	
		J Immunol, 154(5):2358-2365	
	(19	(1995); and, Grunstein MM, et	

				al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154- L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.	
59	HBMCI50	1007	Production of IL-8 by by endothelial	Assays measuring production of IL-8 are well known in the	Highly preferred indications include immunological and
			cells (such as	art and may be used or	inflammatory disorders (e.g.,
			Human Umbilical Cord Endothelial	routinely modified to assess the ability of polynentides of	such as allergy, asthma,
			Cells).	the invention (including	below under "Immune
_ <del></del>				antibodies and agonists or	Activity", and "Blood-Related
				antagonists of the invention) to	Disorders"). Highly preferred
				regulate production and/or	indications also includie
				secretion of IL-8. For	autoimmune disorders (e.g.,
				example, FMAT may be used	rheumatoid arthritis, systemic
				or routinely modified to assess	lupus erythematosis, Crohn"s
				the ability of polypeptides of	disease, multiple sclerosis
				the invention (including	and/or as described below),
				antibodies and agonists or	neoplastic disorders (e.g.,
				antagonists of the invention) to	organ cancers such as lung,
				regulate production and/or	liver, colon cancer, and/or as
				secretion of IL-8 from	described below under
				endothelial cells (such as	"Hyperproliferative
				human umbilical vein	Disorders"), and
				endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
				HUVECs are endothelial cells	such as described below under
				which line venous blood	"Cardiovascular Disorders").
_				vessels, and are involved in	Preferred indications include
				functions that include, but are	thrombosis, bacteremia and

not limited to, angiogenesis, vascular vascular permeability, vascular tone, and immune cell extravasation. Endothelial cells play a pivotal role in the initiation and perpetuation of inflammation and secretion of inflammation and secretion of in recruitment and activation of immune cells such as neutrophils, macrophages, and lymphocytes.	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediate humoral or cellmediated immunity.  Exemplary assays that test for immunomodulatory proteins evaluate the production of
not limited to vascular perm tone, and imm extravasation cells play a pi initiation and inflammation IL-8 may play role in recruit activation of such as neutre macrophages. Iymphocytes.	RANTES immunor that inducells, mo eosinoph the art an routinely the ability the invented antibodic antagonis mediate induce chemelate induce chemelate inmunor evaluate evaluate
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1007
	HBMCI50
	65 751

cytokines, such as RANTES, and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells
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				(HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to,	
				angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	
59	HBMCI50	1007	Production of VCAM in	Assays for measuring expression of VCAM are well-	Highly preferred indications include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
75				agonists or antagonists of the	inflammatory disorders.
				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
-				endothelial cells. Endothelial	"Immune Activity", "Blood-
_		-		cells are cells that line blood	Related Disorders",
				vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,

				include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and	breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
09	HBNAW17	1008	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,
SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.		
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malignant glioma), solid tumors, and prostate breast	lung, colon, pancreatic,	esophageal, stomach, brain, liver and uninger, Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication
	.,,																											
			-																									

				The second of th	is infection (e.g., an infectious disease as described below
		7,700			under "Infectious Disease").
	HBNAW17	1008	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
09				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
				routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
_				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
		-		Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
		•		test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
				disclosed in: Shimizu, H., et	diseases and disorders as

al., Endocr J. 47(3):261-9	described in the
 (2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
   17 (1999); Filipsson, K., et al.,	endocrine disorders (as
Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
(1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 271(28):16544-52	neuropathy, vision impairment
(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
Journal of Biomolecular	blindness), ulcers and impaired
Screening, 4:193-204 (1999),	wound healing, and infection
the contents of each of which	(e.g., infectious diseases and
is herein incorporated by	disorders as described in the
 reference in its entirety.	"Infectious Diseases" section
Pancreatic cells that may be	below, especially of the
 used according to these assays	urinary tract and skin), carpal
are publicly available (e.g.,	tunnel syndrome and
through the ATCC) and/or	Dupuytren's contracture).
may be routinely generated.	An additional highly preferred
Exemplary pancreatic cells that	indication is obesity and/or
may be used according to these	complications associated with
assays include HITT15 Cells.	obesity. Additional highly
HITT15 are an adherent	preferred indications include
 epithelial cell line established	weight loss or alternatively,
from Syrian hamster islet cells	weight gain. Additional highly
 transformed with SV40. These	preferred indications are
cells express glucagon,	complications associated with
somatostatin, and	insulin resistance.
glucocorticoid receptors. The	
cells secrete insulin, which is	
stimulated by glucose and	
glucagon and suppressed by	

				somatostatin or	
				glucocorticoids. ATTC# CRL-	
				1777 Refs: Lord and	
				Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
	HBOEG69	1010	Activation of	Assays for the activation of	A preferred embodiment of
62			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
		,		of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),

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boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional	highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid	arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862- 3873 (1994); and Black et al., Virus Genes 12(2):105-117	(1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be	used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	

					example, hyperplasia,
-					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
· ·					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
•					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
			on it is a debat of the control of t	10.0000mm	under "Infectious Disease").
	HBXFL29	1011	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
63			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred

indications include immune	and hematopoietic disorders	(e.g., as described below under	"Immune Activity", and	"Blood-Related Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting or inhibiting	immune cell proliferation.	Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include boosting an	eosinophil-mediated immune	response, and suppressing an	eosinophil-mediated immune	response.					
to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to promote or	inhibit cell proliferation,	activation, and apoptosis.	Exemplary assays for JNK	kinase activity that may be	used or routinely modified to	test JNK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.
	in an																													

Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J
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			Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N- terminal kinase and failure of prednisolone to inhibit JUN N- terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents	
			of each of which are herein incorporated by reference in its entirety.	
 HCACU58	1012	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
	,	as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate the serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth. Exemplary assays	Activity", "Blood-Related
			for transcription through the	Disorders", and/or

"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described	(e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional	inginy preferred indications include inflammation and inflammatory disorders and	treating joint damage in	arthritis. An additional highly	preserved indication is sepsis. Highly preferred indications include neonlastic diseases			highly preferred indications include neoplasms and	cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g.,
SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) include assays disclosed in	(1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,	85:6342-6346 (1988); and	Diack et al., vilus Gelles 12(2):105-117 (1997), the content of each of which are	herein incorporated by	cells that may be used	according to these assays are publicly available (e.g.,	Exemplary mouse T cells that	assays include the CTLL cell	dependent suspension culture of T cells with cytotoxic	activity.	

malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication
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					is infection (e.g., an infectious disease as described below under "Infectious Disease").
64	HCACU58	1012	Activation of transcription	This reporter assay measures activation of the GATA-3	Highly preferred indications include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,
				routinely modified to test	lymphoma, melanoma,
				GATA3-response element	prostate, breast, lung, colon,
				activity of polypeptides of the	pancreatic, esophageal,

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stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.			
invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to	these assays include the HMC-	1 cell line, which is an	immature human mast cell line	established from the peripheral	blood of a patient with mast
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			-																											
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				cell leukemia, and exhibits	
			-	many characteristics of	
				immature mast cells.	
	HCACU58	1012	Production of	Endothelial cells, which are	Highly preferred indications
64			ICAM in	cells that line blood vessels,	include inflammation (acute
			endothelial cells	and are involved in functions	and chronic), restnosis,
			(such as human	that include, but are not limited	atherosclerosis, asthma and
			umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
			endothelial cells	permeability, vascular tone,	indications include
			(HUVEC))	and immune cell extravasation.	inflammation and
				Exemplary endothelial cells	inflammatory disorders,
				that may be used in ICAM	immunological disorders,
_				production assays include	neoplastic disorders (e.g.
				human umbilical vein	cancer/tumorigenesis), and
				endothelial cells (HUVEC),	cardiovascular disorders (such
				and are available from	as described below under
				commercial sources. The	"Immune Activity", "Blood-
				expression of ICAM (CD54),a	Related Disorders",
				intergral membrane protein,	"Hyperproliferative Disorders"
				can be upregulated by	and/or "Cardiovascular
				cytokines or other factors, and	Disorders"). Highly preferred
				ICAM expression is important	indications include neoplasms
				in mediating immune and	and cancers such as, for
				endothelial cell interactions	example, leukemia, lymphoma,
				leading to immune and	melanoma, renal cell
				inflammatory responses.	carcinoma, and prostate,
				Assays for measuring	breast, lung, colon, pancreatic,
				expression of ICAM-1 are	esophageal, stomach, brain,
				well-known in the art and may	liver and urinary cancer. Other
.22				be used or routinely modified	preferred indications include
				to assess the ability of	benign dysproliferative

				including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
64	HCACU58	1012	Production of IL-10 and activation of T-cells.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis

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and/or as described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response.																								
used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including	agonists or antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation

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of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Kinase assay: measures the phosphorylation of Elk-1, an indication of activation of extracellular signal regulated kinase (ERK). ERK pathway regulates cell growth, proliferation and differentiation. Cells were pretreated with SID supernatants for 15-18 hours, and then 100 nM of insulin was added to stimulate ERK kinase. Phosphorylation of Elk-1 was measured after a 20 minute incubation. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used
	Inhibition of adipocyte ERK signaling pathway.
	1013
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HCDAF84 1014 Activation of transcription through GATA-3 response element in immune cells (such as mast cells).		Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders.
	element are well-known in the	include blood disorders (e.g.,
	art and may be used or	as described below under
	routinely modified to assess	"Immune Activity", "Blood-

the ability of polypeptides of	Related Disorders", and/or
the invention (including	"Cardiovascular Disorders").
antibodies and agonists or	Preferred indications include
antagonists of the invention) to	autoimmune diseases (e.g.,
regulate GATA3 transcription	rheumatoid arthritis, systemic
factors and modulate	lupus erythematosis, multiple
expression of mast cell genes	sclerosis and/or as described
important for immune response	below) and
development. Exemplary	immunodeficiencies (e.g., as
assays for transcription	described below). Preferred
through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	described below under
disclosed in Berger et al., Gene	"Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Henderson et al., Mol Cell Biol   (ALL), plasmacytomas,	(ALL), plasmacytomas,

				14(6):4286-4294 (1994), the contents of each of which are	multiple myeloma, Burkitt's lymphoma, arthritis. AIDS.
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HCDAF84	1014	Activation of	This reporter assay measures	Highly preferred indications
99			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
			•	cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-

			used or routinely modified to	Related Disorders", and/or
			assess the ability of	"Cardiovascular Disorders").
			polypeptides of the invention	Preferred indications include
			(including antibodies and	autoimmune diseases (e.g.,
			agonists or antagonists of the	rheumatoid arthritis, systemic
			invention) to regulate NFAT	lupus erythematosis, multiple
	)		transcription factors and	sclerosis and/or as described
			modulate expression of genes	below) and
			involved in	immunodeficiencies (e.g., as
			immunomodulatory functions.	described below). Preferred
			Exemplary assays for	indications include neoplastic
			transcription through the	diseases (e.g., leukemia,
			NFAT response element that	lymphoma, melanoma,
			may be used or routinely	prostate, breast, lung, colon,
			modified to test NFAT-	pancreatic, esophageal,
			response element activity of	stomach, brain, liver, and
			polypeptides of the invention	urinary tract cancers and/or as
-			(including antibodies and	described below under
			agonists or antagonists of the	"Hyperproliferative
			invention) include assays	Disorders"). Other preferred
-			disclosed in Berger et al., Gene	indications include benign
			66:1-10 (1998); Cullen and	dysproliferative disorders and
.,			Malm, Methods in Enzymol	pre-neoplastic conditions, such
			216:362-368 (1992); Henthorn	as, for example, hyperplasia,
			et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
			85:6342-6346 (1988); De Boer	Preferred indications include
		-	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
			31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
			et al., J Immunol	leukemias, Hodgkin's disease,
			165(12):7215-7223 (2000);	acute lymphocytic anemia
			Hutchinson and McCloskey, J	(ALL), plasmacytomas,

				Biol Chem 270(27):16333- 16338 (1995) and Turner et	multiple myeloma, Burkitt's
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
			*	established from the peripheral	
				blood of a patient with mast	
	-			cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HCDAF84	1014	Production of	Endothelial cells, which are	Highly preferred indications
99			ICAM in	cells that line blood vessels,	include inflammation (acute
			endothelial cells	and are involved in functions	and chronic), restnosis,
			(such as human	that include, but are not limited	atherosclerosis, asthma and
***			umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
		<u></u>	endothelial cells	permeability, vascular tone,	indications include
			(HUVEC))	and immune cell extravasation.	inflammation and
				Exemplary endothelial cells	inflammatory disorders,
				that may be used in ICAM	immunological disorders,
				production assays include	neoplastic disorders (e.g.
				human umbilical vein	cancer/tumorigenesis), and

cardiovascular disorders (such	as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred	indications include neoplasms	and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell	carcinoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.										
endothelial cells (HUVEC),	and are available from	commercial sources. The	expression of ICAM (CD54),a	intergral membrane protein,	can be upregulated by	cytokines or other factors, and	ICAM expression is important	in mediating immune and	endothelial cell interactions	leading to immune and	inflammatory responses.	Assays for measuring	expression of ICAM-1 are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate ICAM-1	expression. Exemplary assays	that may be used or routinely	modified to measure ICAM-1	expression include assays	disclosed in: Rolfe BE, et al.,	Atherosclerosis, 149(1):99-110	(2000); Panettieri RA Jr, et al.,	J Immunol, 154(5):2358-2365	(1995); and, Grunstein MM, et	al., Am J Physiol Lung Cell
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								,									and the second													

Mol Physiol, 278(6):L1154- L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.	RANTES FMAT. Assays for immunomodulatory proteins	that induce chemotaxis of T cells, monocytes, and	eosinophils are well known in	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention
	Production of RANTES in	endothelial cells (such as human	umbilical vein endothelial cells	(HUVEC))																			
	1014																						
	HCDAF84																	-					
	99																						

(including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J	204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995);	Immunol 101(3):398-407 (1995), the contents of each of which are herein incorporated	Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC).	that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line	venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone,
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	HCDAF84	1014	Production of	Assays for measuring	Highly preferred indications
99			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
		,	(HUVEC))	(including antibodies and	inflammation and
		-		agonists or antagonists of the	inflammatory disorders,
				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
•				vessels, and are involved in	"Hyperproliferative Disorders"
-				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
				endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
				expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic
				associated protein, can be	conditions, such as, for
				upregulated by cytokines or	example, hyperplasia,

HCE1Q89	1015	Production of IFNgamma using a T cells	other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses. IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and	A highly preferred embodiment of the invention includes a method for stimulating the production of IENA An alternative highly
			inhibits TH2 differentiation; promotes 1gG2a and inhibits lgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to	preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with
			assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly

preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described	below), immunodeficiency (e.g., as described below),	boosting a T cell-mediated	suppressing a T cell-mediated	immune response. Additional	highly preferred indications include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other
immunomodulation, regulate inflammatory activities, modulate TH2 helper cell	function, and/or mediate humoral or cell-mediated	immunity. Exemplary assays that test for	immunomodulatory proteins	evaluate use production of cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad	Sci 856:22-32 (1998); Boehm	et al., Annu Rev Immunol	15:749-795 (1997), and	Rheumatology (Oxford)
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				38(3):214-20 (1999), the	preferred indications include
-				contents of each of which are	benign dysproliferative
				herein incorporated by	disorders and pre-neoplastic
		_		reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
,				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
		-		be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
( )	HCE2F54	1016	Regulation of	Assays for the regulation of	A highly preferred
89			transcription	transcription through the	indication is diabetes mellitus.
			through the PEPCK	PEPCK promoter are well-	An additional highly preferred
			promoter in	known in the art and may be	indication is a complication
			hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease

(Inclu	(including antibodies and	(e.g., renal failure,
agonii	agonists or antagonists of the	nephropathy and/or other
invent	invention) to activate the	diseases and disorders as
PEPC	PEPCK promoter in a reporter	described in the "Renal
constr	construct and regulate liver	Disorders" section below),
ioanig gincoi	gluconeogenesis. Exemplary	diabetic neuropathy, nerve
assays	assays for regulation of	disease and nerve damage
transc	transcription through the	(e.g., due to diabetic
PEPC	PEPCK promoter that may be	neuropathy), blood vessel
o pesn	used or routinely modified to	blockage, heart disease, stroke,
test fo	test for PEPCK promoter	impotence (e.g., due to diabetic
activit	activity (in hepatocytes) of	neuropathy or blood vessel
polype	polypeptides of the invention	blockage), seizures, mental
(inclu	(including antibodies and	confusion, drowsiness,
agonis	agonists or antagonists of the	nonketotic hyperglycemic-
invent	invention) include assays	hyperosmolar coma,
disclo	disclosed in Berger et al., Gene	cardiovascular disease (e.g.,
1-1:99	66:1-10 (1998); Cullen and	heart disease, atherosclerosis,
Malm	Malm, Methods in Enzymol	microvascular disease,
216:36	216:362-368 (1992); Henthorn	hypertension, stroke, and other
et al.,	et al., Proc Natl Acad Sci USA	diseases and disorders as
759:63	85:6342-6346 (1988);	described in the
Lochh	Lochhead et al., Diabetes	"Cardiovascular Disorders"
49(6):8	49(6):896-903 (2000); and	section below), dyslipidemia,
Yeagle	Yeagley et al., J Biol Chem	endocrine disorders (as
275(23)	275(23):17814-17820 (2000),	described in the "Endocrine
the coi	the contents of each of which	Disorders" section below),
is here	is herein incorporated by	neuropathy, vision impairment
referer	reference in its entirety.	(e.g., diabetic retinopathy and
Hepatc	Hepatocyte cells that may be	blindness), ulcers and impaired
used a	used according to these assays	wound healing, infection (e.g.,

an infectious diseases or disorders as described in the "Infectious Diseases" section below, especially of the	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or	complications associated with obesity. Additional highly preferred indications include	weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with	Additional highly preferred indications are disorders of the musculoskeletal systems	including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred	indications include glycogen storage disease (e.g., glycogenoses), hepatitis, gallstones, cirrhosis of the	liver, degenerative of necrouc liver disease, alcoholic liver diseases, fibrosis, liver
are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary liver hepatoma	according to these assays include H4lle cells, which contain a tyrosine amino transferase that is inducible	with glucocorticoids, insulin, or cAMP derivatives.					
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regeneration, metabolic	disease, dyslipidemia and	cholesterol metabolism, and	hepatocarcinomas.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), infection	(e.g., an infectious disease	and/or disorder as described	below under "Infectious	Disease"), endocrine disorders	(e.g., as described below under	"Endocrine Disorders"), and	neural disorders (e.g., as	described below under "Neural	Activity and Neurological	Diseases").	Additional preferred	indications include neoplastic	diseases (e.g., as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, leukemia,
									-													-								
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											-			-																

lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	
	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of epithhelial genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element
	Activation of transcription through NFKB response element in epithelial cells (such as HELA cells).
	1016
	HCE2F54
	89

780				the invention) include assays disclosed in: Kaltschmidt B, et al., Oncogene, 18(21):3213-3225 (1999); Beetz A, et al., Int J Radiat Biol, 76(11):1443-1453 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the HELA cell	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include include inflammation and inflammatory disorders.
	HCE2E44	1016	Inhihition of	Ime.	
89	HCEZF34	1016	Inhibition of	Reporter Assay: construct	
00			squalene synthetase	contains regulatory and coding	

sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose
gene transcription.	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1016
	HCE2F54
	89

cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on	quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells develoned	through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	This reporter assay measures activation or inhibition of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation or inhibition of transcription through the NFKB response element are well-known in the art and may be used or
			Activation or inhibition of transcription through NFKB response element in immune cells (such as basophils).
	·		1016
,			HCE2F54
			89

routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	regulate NFKB transcription factors and modulate expression of immunomodulatory genes.	pathogenesis of asthma.  Exemplary assays for transcription through the	may be used or rountinely modified to test NFKB-	response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Marone et al, Int Arch Allergy	(1997), the contents of each of which are herein incorporated
				1,00			

	SID	r 15-	nL	ulate		r 48	. pe	says			- 1			-	with		ė.	can	into	hi et			72),	are			Highly preferred indications		inflammatory disorders.	
by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-	18 hours, and then 10 ng/mL	of TNF was added to stimulate	the NFkB reporter. SEAP	activity was measured after 48	hours. Basophils that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous	leukemia. It is an immature	prebasophilic cell line that can	be induced to differentiate into	mature basophils. See, Kishi et	al., Leuk Res. 9:381-390	(1985); Blom et al., Eur J	Immunol. 22:2025-32 (1992),	where the contents of each are	herein incorporated by	reference in its entirety.	This assay uses a NFKB	response element (which will	bind NFKB transcription	factors) linked to a renorter
					•								-				-7-										Activation of	transcription	through NFKB	response element in
																					<u></u>						1016			
																											HCE2F54			
																											Ç	89		

	immune cells (such	gene to measure NFKB	include immunological and
	as the U937 human	mediated transcription in the	hematopoietic disorders (e.g.,
	monocyte cell line).	human monocyte cell line	as described below under
-		U937. NFKB is upregulated	"Immune Activity", "Blood-
		by cytokines and other factors	Related Disorders", and/or
		and NFKB element activation	"Cardiovascular Disorders").
		leads to expression of	Highly preferred indications
		immunomodulatory genes.	include autoimmune diseases
		Activation of NFKB in	(e.g., rheumatoid arthritis,
-		monocytes can play a role in	systemic lupus erythematosis,
		immune responses. Exemplary	multiple sclerosis and/or as
		assays for transcription	described below), and
		through the NFKB response	immunodeficiencies (e.g., as
		element that may be used or	described below). An
		rountinely modified to test	additional highly preferred
		NFKB-response element	indication is infection (e.g.,
		activity of polypeptides of the	AIDS, and/or an infectious
		invention (including antibodies	disease as described below
		and agonists or antagonists of	under "Infectious Disease").
		the invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
	-	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Valle	Disorders"). Highly preferred
		Blazquez et al, Immunology	indications include neoplasms
		90(3):455-460 (1997);	and cancers, such
		Aramburau et al., J Exp Med	as,melanoma, renal cell
		82(3):801-810 (1995); and	carcinoma, leukemia,
		Fraser et al., 29(3):838-844	lymphoma, and prostate,

				(1999), the contents of each of which are herein incorporated	breast, lung, colon, pancreatic, esophageal, stomach, brain,
4				by reference in its entirety. Monocytic cells that may be	liver and urinary cancer. Other preferred indications include
				used according to these assays	benign dysproliferative
				are publicly available (e.g.,	disorders and pre-neoplastic
				through the ATCC).	conditions, such as, for
		-		Exemplary human monocyte	example, hyperplasia,
				cells that may be used	metaplasia, and/or dysplasia.
				according to these assays	Preferred indications also
				include the U937 cell line,	include anemia, pancytopenia,
				which is cell line derived by	leukopenia, thrombocytopenia,
			-	Sundstrom and Nilsson in	Hodgkin's disease, acute
				1974 from malignant cells	lymphocytic anemia (ALL),
				obtained from the pleural	plasmacytomas, multiple
				effusion of a patient with	myeloma, Burkitt's lymphoma,
				histiocytic lymphoma.	arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HCEFB80	1017	Activation of	Assays for the activation of	Highly preferred indications
69			transcription	transcription through the	include neoplastic diseases
		•	through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below

immune cells (such are well-known in the art and nade "Hyperprolificative may be used or routinely indications include neoplasms of politypeptides of the invention (including antibodies example, leukemia, lymphoma and agonists or antagonists of antagonists of the invention) to regulate the invention of regulate gene expression involved in a vide variety of breast, lung, colon, panceatic, ell functions. Exemplary element and agonists or antagonists of the colon, panceatic, assays for transcription feactors and formation assays for transcription element that may be used or preferred indications include countinely modified to test of polypeptides of the invention (including antibodies enema activity disorders and prostate, disolosed in Bergonist of Astropouse element activity disorders and prostate, and agonists or antagonists of metaplasia, and agonists or antagonists of metaplasia, and disolosed in Berger et al., Gene autoimmune diseases (e.g., 66:1-10 (1998); Henthon and Hentimen et al., Blood immune response, and element et al., Gene autoimmune second element contents of each (1998); Henthon selectoris and or a rell-mediated inficiations include assistance of polypeptides of the invention include assays and entitivity and hentimen et al., Gene autoimmune response, additional contents of each of which are preferred indications include assistances.
immune cells (such as T-cells).

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inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	with "Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted
herein incorporated by	reference in its entirety.	Exemplary mouse T cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary T cells that may be	used according to these assays	include the CTLL cell line,	which is a suspension culture	of IL-2 dependent cytotoxic T	cells.																			
	•			-																						41.				
							1														-									

					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
69	HCEFB80	1017	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or	A highly preferred indication is diabetes mellitus. An additional highly preferred
				the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease
				stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies.	nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),
				Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and	diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,
				disregulation is a key component in diabetes.  Exemplary assays that may be used or routinely modified to test for stimulation of insulin	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-
				secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of	hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,

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	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocriné disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional highly	preferred indications are	complications associated with	insulin resistance.		
	the invention) include assays	disclosed in: Shimizu, H., et	al., Endocr J, 47(3):261-9	(2000); Salapatek, A.M., et al.,	Mol Endocrinol, 13(8):1305-	17 (1999); Filipsson, K., et al.,	Ann N Y Acad Sci, 865:441-4	(1998); Olson, L.K., et al., J	Biol Chem, 271(28):16544-52	(1996); and, Miraglia S et. al.,	Journal of Biomolecular	Screening, 4:193-204 (1999),	the contents of each of which	is herein incorporated by	reference in its entirety.	Pancreatic cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary pancreatic cells that	may be used according to these	assays include HITT15 Cells.	HITT15 are an adherent	epithelial cell line established	from Syrian hamster islet cells	transformed with SV40. These	cells express glucagon,	somatostatin, and	glucocorticoid receptors. The	celle secrete insuling which is
77.5							·																				No. of the last of				

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays
	Production of ICAM-1
	1018
	HCEGR33
	70

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or	antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for	example, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neonlastic conditions, such
are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may	be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of epithhelial genes. Exemplary assays for transcription through the NFKB response element that may be used or	NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Kaltschmidt B, et al., Oncogene, 18(21):3213-
	Activation of transcription through NFKB response element in	epithelial cells (such as HELA cells).	
	HCEMP62 1019		
	71		

3225 (1999); Beetz A, et al., Int J Radiat Biol, 76(11):1443- 1453 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the HELA cell line.		ement in factors) linked to a reporter Highly preferred indications lls (such gene to measure NFKB include immunological and
	HCEMP62 1019 Activation of transcription through NFKB	immune cells (such

	monocyte cell line).	human monocyte cell line	as described below under
		U937. NFKB is upregulated	"Immune Activity", "Blood-
		by cytokines and other factors	Related Disorders", and/or
		and NFKB element activation	"Cardiovascular Disorders").
		leads to expression of	Highly preferred indications
		immunomodulatory genes.	include autoimmune diseases
		Activation of NFKB in	(e.g., rheumatoid arthritis,
		monocytes can play a role in	systemic lupus erythematosis,
		immune responses. Exemplary	multiple sclerosis and/or as
		assays for transcription	described below), and
		through the NFKB response	immunodeficiencies (e.g., as
		element that may be used or	described below). An
		rountinely modified to test	additional highly preferred
		NFKB-response element	indication is infection (e.g.,
		activity of polypeptides of the	AIDS, and/or an infectious
		invention (including antibodies	disease as described below
		and agonists or antagonists of	under "Infectious Disease").
		the invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Valle	Disorders"). Highly preferred
		Blazquez et al, Immunology	indications include neoplasms
		90(3):455-460 (1997);	and cancers, such
		Aramburau et al., J Exp Med	as,melanoma, renal cell
		82(3):801-810 (1995); and	carcinoma, leukemia,
		Fraser et al., 29(3):838-844	lymphoma, and prostate,
		(1999), the contents of each of	breast, lung, colon, pancreatic,
72.		which are herein incorporated	esophageal, stomach, brain,

	l) Jo	of the invention (including	invention includes a method
	anti	antibodies and agonists or	for inhibiting endothelial cell
	anta	antagonists of the invention) to	growth. A highly preferred
	inhi	inhibit caspase protease-	embodiment of the invention
-	mec	mediated apoptosis.	includes a method for
	Exe	Exemplary assays for caspase	stimulating endothelial cell
	apol	apoptosis that may be used or	proliferation. An alternative
-	rout	routinely modified to test	highly preferred embodiment
	casi	caspase apoptosis rescue of	of the invention includes a
	lod	polypeptides of the invention	method for inhibiting
	(inc	(including antibodies and	endothelial cell proliferation.
	agol	agonists or antagonists of the	A highly preferred
	inve	invention) include the assays	embodiment of the invention
	disc	disclosed in Romeo et al.,	includes a method for
	Car	Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
	(200	(2000); Messmer et al., Br J	growth. An alternative highly
	Pha	Pharmacol 127(7): 1633-1640	preferred embodiment of the
	(199	(1999); and J Atheroscler	invention includes a method
	Thr	Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
	the	the contents of each of which	growth. A highly preferred
	are	are herein incorporated by	embodiment of the invention
	refe	reference in its entirety.	includes a method for
	End	Endothelial cells that may be	stimulating apoptosis of
	) asc	used according to these assays	endothelial cells. An
	are	are publicly available (e.g.,	alternative highly preferred
	thro	through commercial sources).	embodiment of the invention
	Exe	Exemplary endothelial cells	includes a method for
	that	that may be used according to	inhibiting (e.g., decreasing)
	thes	these assays include bovine	apoptosis of endothelial cells.
	aort	aortic endothelial cells	A highly preferred
	(bA	(bAEC), which are an example	embodiment of the invention

of endothelial cells which line	includes a method for
blood vessels and are involved	stimulating angiogenisis. An
in functions that include, but	alternative highly preferred
are not limited to,	embodiment of the invention
angiogenesis, vascular	includes a method for
permeability, vascular tone,	inhibiting angiogenesis. A
and immune cell extravasation.	highly preferred embodiment
	of the invention includes a
	method for reducing cardiac
	hypertrophy. An alternative
	highly preferred embodiment
	of the invention includes a
	method for inducing cardiac
	hypertrophy. Highly
	preferred indications include
	neoplastic diseases (e.g., as
	described below under
	"Hyperproliferative
	Disorders"), and disorders of
	the cardiovascular system
	(e.g., heart disease, congestive
	heart failure, hypertension,
	aortic stenosis,
	cardiomyopathy, valvular
	regurgitation, left ventricular
	dysfunction, atherosclerosis
	and atherosclerotic vascular
	disease, diabetic nephropathy,
	intracardiac shunt, cardiac
	hypertrophy, myocardial
	infarction, chronic

hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include, cardiovascular	endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as	well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly	preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.	include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications	such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis,

hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease,	such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's disease and Reynaud's phenomenom, aneurysms,	restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease,
		<u>.</u>			;

and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood
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				•																	<del></del>									
				_						- 15													-							

disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma,
Properties and the properties of the properties	Assays for the activation of transcription through the Gamma Interferon Activation  Site (GAS) response element an are well-known in the art and may be used or routinely Dimodified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of (e.
	Activation of Assa transcription trans through GAS Gam response element in Site (immune cells (such are w as T-cells). may modi of po inver and a
	1020
	HCENK38
	72

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Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral	infections, tuberculosis, infections associated with	chronic granulomatosus disease and malignant	osteoporosis, and/or an	infectious disease as described	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease, and	asthma and allergy.	A highly preferred
Exemplary T cells that may be used according to these assays include the CTLL cell line.	which is a suspension culture of IL-2 dependent cytotoxic T	cells.																							Kinase assay. Kinase assays,
																									Activation of
																									1020
																									HCENK38
						_																			

embodiment of the invention includes a method for stimulating hepatocyte cell proliferation. An alternative	highly preferred embodiment of the invention includes a method for inhibiting hepatocyte cell proliferation.  A highly preferred embodiment of the invention includes a method for the invention discussed.	differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting hepatocyte cell differentiation. A highly preferred embodiment of the invention includes a method for activating hepatocyte cells. An	
for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation	are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit on modification	activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the	assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein
Hepatocyte ERK Signaling Pathway			
72			

Disorders"). Preferred indications include neoplastic diseases (e.g., as described	below under "Hyperproliferative	Disorders"), blood disorders	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related Disorders"). immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),
incorporated by reference in its entirety. Rat liver hepatoma cells that may be used	according to these assays are publicly available (e.g.,	through the ATCC).  Exemplary rat liver henatoma	cells that may be used	according to these assays	include H4lle cells, which are known to respond to	glucocorticoids, insulin, or	cAMP derivatives.																		
																-									

diabetic neuropathy, nerve disease and nerve damage	neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,	hyperosmolar coma, cardiovascular disease, atherosclerosis,	microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal
				,		

_			tunnel syndrome and
-			Dumington, a contraction
			Dupuytren s contracture).
			An additional highly preferred
	-		indication is obesity and/or
-			complications associated with
			obesity. Additional highly
			preferred indications include
			weight loss or alternatively,
			weight gain. Additional
			highly preferred indications are
		- 47	complications associated with
			insulin resistance.
			Additonal highly preferred
			indications are disorders of the
	-		musculoskeletal systems
•	_		including myopathies,
	<u></u>		muscular dystrophy, and/or as
		• • • • • • • • • • • • • • • • • • • •	described herein.
			Additional highly preferred
			indications include, hepatitis,
			jaundice, gallstones, cirrhosis
		**	of the liver, degenerative or
		-	necrotic liver disease,
<u>:</u>			alcoholic liver diseases,
			fibrosis, liver regeneration,
-			metabolic disease,
			dyslipidemia and chlolesterol
		***	metabolism.
	-		Additional highly preferred
		-	indications include neoplasms
			and cancers, such as,

hepatocarcinomas, other liver cancers, and colon and pancreatic cancer. Preferred indications also include prostate, breast, lung, esophageal, stomach, brain, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of
	Production of ICAM-1
	1021
	HCEWE17
	<u>د</u> 217

				each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	
47	HCEWE20	1022	Regulation of transcription of Malic Enzyme in hepatocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel

	transcription factors	conflicion drougings
	י בי ייייייייייייייייייייייייייייייייי	contrasion, arowsiness,
	Exemplary assays that may be	nonketotic hyperglycemic-
	used or routinely modified to	hyperosmolar coma,
	test for regulation of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	heart disease, atherosclerosis,
	(in hepatocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment
-	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	wound healing, and infection
	al., J Biol Chem,	(e.g., infectious diseases and
	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the
	Methods in Enzymol.	urinary tract and skin), carpal
	216:362–368 (1992), the	tunnel syndrome and
	contents of each of which is	Dupuytren's contracture).
	herein incorporated by	An additional highly preferred
	reference in its entirety.	indication is obesity and/or
	Hepatocytes that may be used	complications associated with
	according to these assays are	obesity. Additional highly
	publicly available (e.g.,	preferred indications include
	through the ATCC) and/or	weight loss or alternatively,

weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
may be routinely generated. Exemplary hepatocytes that may be used according to these assays includes the mouse 3T3-L1 cell line. 3T3-L1 is a mouse preadipocyte cell line (adherent). It is a continuous substrain of 3T3 fibroblasts developed through clonal isolation. Cells undergo a preadipocyte to adipose-like conversion under appropriate differentiation culture conditions.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365
	Production of ICAM-1
	1022
	HCEWE20
	74

				al., Am J Physiol Lung Cell Mol Physiol 278(6):11154-	
				L1163 (2000), the contents of each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				through the ATCC) and/or	
	<del></del>			may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include Aortic Smooth Muscle	
				Cells (AOSMC); such as	
				bovine AOSMC.	
	HCFMV71	1024	Activation of	Assays for the activation of	Preferred indications
9/			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are known in	(e.g., as described below under
			response element in	the art and may be used or	"Hyperproliferative
			immune cells (such	routinely modified to assess	Disorders"), blood disorders
			as T-cells).	the ability of polypeptides of	(e.g., as described below under
				the invention (including	"Immune Activity",
				antibodies and agonists or	"Cardiovascular Disorders",
				antagonists of the invention) to	and/or "Blood-Related
				modulate growth and other cell	Disorders"), and infection
				functions. Exemplary assays	(e.g., an infectious disease as
				for transcription through the	described below under
				AP1 response element that	"Infectious Disease"). Highly
				may be used or routinely	preferred indications include
				modified to test AP1-response	autoimmune diseases (e.g.,

rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and imminodeficiencies (e.g. as imminodeficiencies (e.g. as	described below). Additional highly preferred indications include inflammation and inflammatory disorders.	Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under	"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia,
element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol	18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by	reference in its entirety.  Mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary mouse T cells that may be used according to these assays include the HT2 cell line, which is an IL-2 dependent suspension culture cell line that also responds to IL-4.
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leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and
	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, bind to CREB transcription factor, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription through the cAMP response element that may be used or routinely
	Activation of transcription through cAMP response element in immune cells (such as T-cells).
	1024
	HCFMV71
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suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below	under "Hyperpronneranve Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia,	lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's	disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and	urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia,
response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J	Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T	cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension	culture of leukemia cells that produce IL-2 when stimulated.
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(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	Highly preferred indications include neoplastic diseases  (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, and prostate, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include
	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or
	Activation of transcription through GAS response element in immune cells (such as T-cells).
	1024
	HCFMV71
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routinely modified to test disorders and pre-neoplastic of polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene disclosed in Berger et al., Gene disclosed in Berger et al., Gene de 1. Proc Natl Acad Sci USA Malm, Methods in Enzymol sclerosis and/or as described et al., Proc Natl Acad Sci USA Matikainen et al., Blood Hentinen et al., Blood immune response, and Hentinen et al., J Immunol 155(10):4582-4587 (1995); the immune response, and suppressing a T cell-mediated inflammation and suppressing a T cell-mediated inflammation and suppressing a T cell-mediated inflammation and inflammatory disorders. Exemplary human T cells, inflammatory disorders. Exemplary human T cells, include blood disorders (e.g., through the assays are publicly available (e.g., through the Related Disorders"), and infections associated with chronic granulomatosus disease and malignant	oodies ts of ays Gene and ool ol ol ol ine, ine, ng to le	oodies stand and hol thorn USA ol are i are ine, ine, he is to the hol ol o
routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 83:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety.  Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).

Highly preferred indications include inflammation and inflammatory disorders.  Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or of the "Cardiovascular Disorders").
Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the
Activation of transcription through NFKB response element in immune cells (such as T-cells).
1024
HCFMV71
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	invention) to regulate NFKB	Highly preferred indications
	transcription factors and	include autoimmune diseases
	modulate expression of	(e.g., rheumatoid arthritis,
	immunomodulatory genes.	systemic lupus erythematosis,
	Exemplary assays for	multiple sclerosis and/or as
	transcription through the	described below), and
	NFKB response element that	immunodeficiencies (e.g., as
	may be used or rountinely	described below). An
	modified to test NFKB-	additional highly preferred
	response element activity of	indication is infection (e.g.,
	polypeptides of the invention	AIDS, and/or an infectious
	(including antibodies and	disease as described below
	agonists or antagonists of the	under "Infectious Disease").
	invention) include assays	Highly preferred indications
	disclosed in Berger et al., Gene	include neoplastic diseases
	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	Malm, Methods in Enzymol	lymphoma, and/or as described
-	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Gnes 15(2):105-117	indications include neoplasms
	(1997); and Fraser et al.,	and cancers, such as, for
	29(3):838-844 (1999), the	example, melanoma, renal cell
	contents of each of which are	carcinoma, leukemia,
	herein incorporated by	lymphoma, and prostate,
	reference in its entirety.	breast, lung, colon, pancreatic,
	Exemplary human T cells,	esophageal, stomach, brain,
	such as the MOLT4, that may	liver and urinary cancer. Other
	be used according to these	preferred indications include
	assays are publicly available	benign dysproliferative
	(e.g., through the ATCC).	disorders and pre-neoplastic

					conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia,
					Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory of well disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and alleroy
11	HCFNN01	1025	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method
				the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response	for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood

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disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described	(e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional highly preferred indications	include inflammation and inflammatory disorders, and treating joint damage in	patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma,	under "Hyperproliferative Disorders"). Additionally, highly preferred indications
factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the	SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) include assays disclosed in	(1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992): Henthorn et al.	Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes	12(2):105-117 (1997), the content of each of which are herein incorporated by	reference in its entirety. T cells that may be used according to these assays are	through the ATCC).  Exemplary mouse T cells that	assays include the CTLL cell line, which is an IL-2 dependent suspension culture

of T cells with cytotoxic	include neoplasms and
activity.	cancers, such as, for example
· far race	lankamia lymnhoma
	reukeima, rymphoma,
	melanoma, glioma (e.g.,
1000	malignant glioma), solid
	tumors, and prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic
	conditions, such as, for
	example, hyperplasia,
	metaplasia, and/or dysplasia.
	Preferred indications include
	anemia, pancytopenia,
	leukopenia, thrombocytopenia,
	Hodgkin's disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt's lymphoma,
	arthritis, AIDS, granulomatous
	disease, inflammatory bowel
	disease, neutropenia,
	neutrophilia, psoriasis,
	suppression of immune
	reactions to transplanted
	organs and tissues,
	hemophilia, hypercoagulation,
	diabetes mellitus, endocarditis,

					meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., p. infections).
					disease as described below under "Infectious Disease").
62	HCHNF25	1027	Calcium flux in immune cells (such	Assays for measuring calcium flux are well-known in the art	Preferred embodiments of the invention include using
			as monocytes)	and may be used or routinely	polypeptides of the invention
				modified to assess the ability of polypeptides of the	(or antibodies, agonists, or antagonists thereof) in
				invention (including antibodies	detection, diagnosis,
				and agonists or antagonists of	prevention, and/or treatment of
				the invention) to mobilize	Infection, Inflammation,
				calcium. Cells normally have	Atherosclerosis,
				very low concentrations of	Hypersensitivity, and
				cytosolic calcium compared to	Leukemias
	- 1.0			much higher extracellular	
				calcium. Extracellular factors	
				can cause an influx of calcium,	
				leading to activation of	
				calcium responsive signaling	
				pathways and alterations in	
				cell functions. Exemplary	
				assays that may be used or	
				routinely modified to measure	
				calcium flux in immune cells	
				(such as monocytes) include	
				assays disclosed in: Chan, CC,	
				et al., J Pharmacol Exp Ther,	

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
Andersson, K, et al., Cytokine, 12(12):1784-1787 (2000); Scully, SP, et al., J Clin Invest, 74(2) 589-599 (1984); and, Sullivan, E, et al., Methods Mol Biol, 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated.  Exemplary cells that may be used according to these assays include the THP-1 monocyte cell line.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1
	Production of ICAM-1
	HCMSQ56 1028
	80 80

disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733- 1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgA production and increases IL-6 production. An alternative lgA production (IgA plays a role in mucosal immunity).  IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 highly preferrred indication is disease, plasmacytomas, and chronic myelomas, and chronic participates in IL-6 induces cytotoxic T cells. Teducing) IL-6 production. A has been linked to autoimmune highly preferrred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include hyperproliferative diseases. Plood disorders (e.g., as
expression include assays disclosed in: Takacs P, et FASEB J, 15(2):279-281 (2001); and, Miyamoto K, al., Am J Pathol, 156(5):1 1739 (2000), the contents each of which is herein incorporated by reference entirety. Cells that may be used according to these as are publicly available (e.g through the ATCC) and/o may be routinely generate Exemplary cells that may used according to these as include microvascular endothelial cells (MVEC)	
	Production of IL-6
	1029
	HCMST14
	81

described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,
and differentiation factor	proteins produced by a large	variety of cells where the	expression level is strongly	regulated by cytokines, growth	factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the
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o company	coagaia 1	endocar	yme Dis	erred	tion (e.g	as descr	ctions		erred	e invent	l for	syte	alternativ	mbodim	sepno	ting	ation.	mbodim	scludes	ating	ıtiation.	preferre	e invent	l for	/te	A highly	ment of	s a meth	ġ,	cyte	ernative
bymon	a, 113 per	rellitus,	s, and $\Gamma$	nal pref	is infec	disease	ler "Infe		A highly preferred	ent of th	methoc	g adipo	on. An	ferred e	ention in	r inhibi	prolifer	eferred e	ention ii	or stimu	differer	e highly	ent of th	nethou	adipoc	ation.	embodi	include	lating (e	g) adipo	Analt
hemonbilia hymercoamilation		diabetes mellitus, endocarditis,	meningitis, and Lyme Disease.	An additonal preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Disease")	A hig	embodiment of the invention	includes a method for	stimulating adipocyte	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	adipocyte proliferation.	highly preferred embodiment	of the invention includes	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation.	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative
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									nase assa	k-1 kina	gnal	egulate	fferentia	the art	utinely	the abil	fthe	ng antib	itagonist	promote	ration,	fferentia	for ERI	at may b	modifie	nduced	ptides of	ing antib	itagonist	lude the	n Forrer
									say. Kin	ole an El	ERK si	ion that	ion or di	mown in	sed or ro	to asses:	ptides of	(includi	ists or ar	tion) to J	Il prolife	i, and di	ry assays	tivity tha	outinely	kinase-i	f polype	includ	ists or an	tion) inc	sclosed i
									Kinase assay. Kinase assays,	for example an Elk-1 kinase	assay, for ERK signal	transduction that regulate cell	proliferation or differentiation	are well known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assavs disclosed in Forrer et
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									ion of	Adipocyte ERK	Signaling Pathway	ı																			
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	a	al Biol Chem 379(8-9):1101-	highly preferred embodiment
,		1110 (1998); Le Marchand-	of the invention includes a
	Br	Brustel Y, Exp Clin	method for inhibiting the
-	En	Endocrinol Diabetes	activation of (e.g., decreasing)
	10	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Ky	Kyriakis JM, Biochem Soc	Highly preferred indications
	Sy	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and	and Karin, Nature	(e.g., as described below under
	410	410(6824):37-40 (2001); and	"Endocrine Disorders").
	သိ -	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Bie	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the	the contents of each of which	diseases (e.g., lipomas,
	are	are herein incorporated by	liposarcomas, and/or as
	ref	reference in its entirety.	described below under
	Me	Mouse adipocyte cells that	"Hyperproliferative
	em	may be used according to these	Disorders"). Preferred
	ass	assays are publicly available	indications include blood
	(e.	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Ex	Exemplary mouse adipocyte	congestive heart failure, blood
	[ea]	cells that may be used	vessel blockage, heart disease,
	acc	according to these assays	stroke, impotence and/or as
	inc	include 3T3-L1 cells. 3T3-L1	described below under
	isi	is an adherent mouse	"Immune Activity",
	pre	preadipocyte cell line that is a	"Cardiovascular Disorders",
	000	continuous substrain of 3T3	and/or "Blood-Related
	dit	fibroblast cells developed	Disorders"), immune disorders
	thr	through clonal isolation and	(e.g., as described below under
	un	undergo a pre-adipocyte to	"Immune Activity"), neural
	adi	adipose-like conversion under	disorders (e.g., as described
	ap	appropriate differentiation	below under "Neural Activity
	00	conditions known in the art.	and Neurological Diseases"),

and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as
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described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.
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es a meth	dotnellal ghly prefe	the inven	od for	othelial ce	ı alternati	embodin	includes	iting	proliferat	pa	the inven	od for	otosis of	. An	y preferr	the inven	od for	decreasin	lothelial o	pə.	the inven	od for	ogenisis.	ly preferr	the inven	od for	genesis.
preferred embodiment of the invention includes a method	for inhibiting endothelial cell growth. A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis.
prere inven	for in grow	empo	inclu		prolii	highl	of the	meth	endo	A hig	empc	inclu	stim	endo	alterr	empc	inclu	inhib	apop	A hig	empc	inclu	stim	alteri	empc	inclu	inhib
(including antibodies and	agonists or antagonists of the invention) to promote caspase	protease-mediated apoptosis.	Induction of apoptosis in	endothelial cells supporting the	vasculature of tumors is	associated with tumor	regression due to loss of tumor	blood supply. Exemplary	assays for caspase apoptosis	that may be used or routinely	modified to test capase	apoptosis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3):	209-218 (2000); and Karsan	and Harlan, J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays
(inclu	agoni	protea	Induc	endot	vascu	associ	regres	boold	assay	that n	modif	apopt	polyp	(inclu	agoni	inven	discle	Lett 4	Nor e	209-2	and H	Thror	the co	are he	refere	Endo	nsed
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of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a	method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under		cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiae shunt cardiae.	hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders").	Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic
through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells	(bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but	angiogenesis, vascular permeability, vascular and immune cell extravasation.	,		

disorders that affect vessels	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,
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prostate, breast, lung, colon,	pancreatic, esophageal,	uringry cancer Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and
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atheroschlerotic lesions),	impiant iixation, scarring, ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,
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rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic		sis. Assays for Preferred embodiments of the is are well invention include using polypeptides of the invention of continuous and may be antagonists thereof) in antagonists thereof) in detection, diagnosis, odies and detection, diagnosis, odies and asthma, allergy, and asthma, allergy, inflammation.  Inconnective sues throughout st cells). Mast in connective sues throughout leir activation oulin E -  ed by T helper
			caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E-antigen, promoted by T helper
		·	Regulation of apoptosis of immune cells (such as mast cells).
			1032
			HCNSD93
			84

cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.	Immune cells that may be used	according to these assays are	publicly available (e.g.,
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				through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	
85	HCNSM70	1033	Myoblast cell proliferation	Assays for muscle cell proliferation are well known in the art and may be used or	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of
			,	routinely modified to assess the ability of polypeptides of the invention (including	muscle (such as, rhabdomyoma, and rhabdosarcoma),
				antibodies and agonists or antagonists of the invention) to stimulate or inhibit myoblast	cardiovascular disorders (such as congestive heart failure, cachexia, myxomas, fibromas,
	,			assays for myoblast cell proliferation that may be used or routinely modified to test	congenital caldiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, vascular disease, and
			,	activity of polypeptitues and antibodies of the invention (including agonists or antagonists of the invention) include, for example, assays	also as uescribed below under "Cardiovascular Disorders"), stimulating myoblast proliferation, and inhibiting myoblast proliferation.
		•	·	disclosed in: Soeta, C., et al. "Possible role for the c-ski gene in the proliferation of myogenic cells in regenerating skeletal muscles of rats" Dev	
				Growth Differ Apr;43(2):155-64 (2001); Ewton DZ, et al.,	

single by the set of t	of Highly preferred indications include blood disorders (e.g.,	ed T as described below under ement "Immune Activity", "Blood-
"IGF binding proteins-4, -5 and -6 may play specialized roles during L6 myoblast proliferation and differentiation" J Endocrinol Mar;144(3):539-53 (1995); and, Pampusch MS, et al., "Effect of transforming growth factor beta on proliferation of L6 and embryonic porcine myogenic cells" J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in	differentiation media. Assays for the activation of transcription through the	Nuclear Factor of Activated T cells (NFAT) response element
	Activation of transcription	through NFAT response element in
	1034	
	HCOOS80	
	98	

	immune cells (such	are well-known in the art and	Related Disorders", and/or
	as natural killer		"Cardiovascular Disorders").
	cells).	modified to assess the ability	Highly preferred indications
		of polypeptides of the	include autoimmune diseases
		invention (including antibodies	(e.g., rheumatoid arthritis,
		and agonists or antagonists of	systemic lupus erythematosis,
		the invention) to regulate	multiple sclerosis and/or as
		NFAT transcription factors and	described below),
		modulate expression of genes	immunodeficiencies (e.g., as
		involved in	described below), boosting a T
		immunomodulatory functions.	cell-mediated immune
		Exemplary assays for	response, and suppressing a T
		transcription through the	cell-mediated immune
		NFAT response element that	response. Additional highly
		may be used or routinely	preferred indications include
		modified to test NFAT-	inflammation and
		response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
		agonists or antagonists of the	infectious disease as described
		invention) include assays	below under "Infectious
		disclosed in Berger et al., Gene	Disease"). Preferred
		66:1-10 (1998); Cullen and	indications include neoplastic
		Malm, Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988);	"Hyperproliferative
		Aramburu et al., J Exp Med	Disorders"). Preferred
		182(3):801-810 (1995); De	indications include neoplasms
		Boer et al., Int J Biochem Cell	and cancers, such as, for
The state of the s		Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,

				Fraser et al., Eur J Immunol	and prostate, breast, lung,
				29(3):838-844 (1999); and	colon, pancreatic, esophageal,
				Yeseen et al., J Biol Chem	stomach, brain, liver and
				268(19):14285-14293 (1993),	urinary cancer. Other preferred
				the contents of each of which	indications include benign
				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. NK	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human NK cells	leukopenia, thrombocytopenia,
				that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
					disease, sepsis, neutropenia,
-					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
*****					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HCUBS50	1035	Activation of	Assays for the activation of	Highly preferred indications
87			transcription	transcription through the	include asthma, allergy,
			through GAS	Gamma Interferon Activation	hypersensitivity reactions,
			response element in	Site (GAS) response element	inflammation, and

	immune cells (such	are well-known in the art and	inflammatory disorders.	
	as eosinophils).	may be used or routinely	Additional highly preferred	
		modified to assess the ability	indications include immune	
		of polypeptides of the	and hematopoietic disorders	
		invention (including antibodies	(e.g., as described below under	
		and agonists or antagonists of	"Immune Activity", and	
		the invention) to modulate	"Blood-Related Disorders"),	
		gene expression (commonly	autoimmune diseases (e.g.,	
-		via STAT transcription factors)	rheumatoid arthritis, systemic	
		involved in a wide variety of	lupus erythematosis, Crohn"s	
		cell functions. Exemplary	disease, multiple sclerosis	
		assays for transcription	and/or as described below),	
		through the GAS response	immunodeficiencies (e.g., as	
		element that may be used or	described below), boosting an	
		routinely modified to test	eosinophil-mediated immune	_
		GAS-response element activity	response and, alternatively,	
	· · · · · · · · · · · · · · · · · · ·	of polypeptides of the	suppressing an eosinophil-	
		invention (including antibodies	mediated immune response.	
		and agonists or antagonists of		
		the invention) include assays		
		disclosed in Berger et al., Gene		
		66:1-10 (1998); Cullen and		
		Malm, Methods in Enzymol		
		216:362-368 (1992); Henthorn		
		et al., Proc Natl Acad Sci USA		
		85:6342-6346 (1988);		
,		Matikainen et al., Blood		
		93(6):1980-1991 (1999); and		
		Henttinen et al., J Immunol		
		155(10):4582-4587 (1995); the		
		contents of each of which are		

herein incorporated by reference in its entirety.  Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate or inhibit activation of immune cells include assays disclosed andor eited in: Mayumi M., "EoL-1, a human eosinophilic cell line" Leuk Lymphona; Jun; (3):243-50 (1992); Bhattacharya S., "Granulocyte marcophage colony- stimulating factor and interleukin-5 activate STAT5 and induce CISI mRNA in human peripheral blood eosinophils" Am J Respir Cell Mol Biol, Mar; 24(3):312-6 (2001); and, Du J, et al., "Engagement of the Crk. adapter in interleukin-5 signaling in eosinophils" J Biol Chem; Oct 20;275(42):33167- 75 (2000); the contents of each of which are herein																															
	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to activate or	inhibit activation of immune	cells include assays disclosed	and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interleukin-5	signaling in eosinophils" J Biol	Chem; Oct 20;275(42):33167-	75 (2000); the contents of each	of which are herein	incorporated by reference in its
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		Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include
entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory	response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that
		Activation of transcription through AP1 response element in immune cells (such as T-cells).
		1035
		HCUBS50
		87

autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described	immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders	Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described	below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia,	lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS,
modified to test AP1-response element activity of polypeptides of the invention (including antibodies and	invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997);	Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are	herein incorporated by reference in its entirety.  Mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary mouse T cells that	may be used according to these assays include the HT2 cell line, which is an IL-2 dependent suspension culture cell line that also responds to

allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation.
IL-4.	Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to inhibit caspase proteasemediated apoptosis. Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis rescue of polypeptides of the invention (including antibodies and agonists or antagonists of the
	Protection from Endothelial Cell Apoptosis.
	1036
	HCUCK44
	& &

embodiment of the invention	includes a method for	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting endothelial cell	growth. A highly preferred		includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a
invention) include the assays	disclosed in Romeo et al.,	Cardiovasc Kes 45(3): 788-794	(2000); Messmer et al., Br J	Pharmacol 127(7): 1633-1640	(1999); and J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.					
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method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under	"Hyperproliterative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension,	aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac	hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications	endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins

and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign
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dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal
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diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as
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					described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
<b>&amp;</b>	HCUCK44	1036	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for immunomodulatory proteins	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)  MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing)  MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred inflammation and inflammatory disorders.
				evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-

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colla Chartage and Land	INCIDENT DISOLUCIS, AIM OF
 cens. Such assays that may be	Cardiovascular Disorders").
used or routinely modified to	Highly preferred indications
test immunomodulatory and	include autoimmune diseases
diffferentiation activity of	(e.g., rheumatoid arthritis,
 polypeptides of the invention	systemic lupus erythematosis,
(including antibodies and	multiple sclerosis and/or as
agonists or antagonists of the	described below) and
invention) include assays	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
 45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
 158:2919-2925 (1997), the	disease, inflammatory bowel
 contents of each of which are	disease, sepsis, neutropenia,
herein incorporated by	neutrophilia, psoriasis,
reference in its entirety.	suppression of immune
Human dendritic cells that may	reactions to transplanted
be used according to these	organs and tissues,
assays may be isolated using	hemophilia, hypercoagulation,
techniques disclosed herein or	diabetes mellitus, endocarditis,
 otherwise known in the art.	meningitis (bacterial and
 Human dendritic cells are	viral), Lyme Disease, asthma,
antigen presenting cells in	and allergy Preferred
suspension culture, which,	indications also include
when activated by antigen	neoplastic diseases (e.g.,

			genes in many cell types.	"Cardiovascular Disorders").
•			Exemplary assays for	Highly preferred indications
			transcription through the SRE	include autoimmune diseases
			that may be used or routinely	(e.g., rheumatoid arthritis,
			modified to test SRE activity	systemic lupus erythematosis,
		_	of the polypeptides of the	Crohn"s disease, multiple
		7	invention (including antibodies	sclerosis and/or as described
	<del></del>		and agonists or antagonists of	below), immunodeficiencies
	_		the invention) include assays	(e.g., as described below),
			disclosed in Berger et al., Gene	boosting a T cell-mediated
			 66:1-10 (1998); Cullen and	immune response, and
			Malm, Methods in Enzymol	suppressing a T cell-mediated
			216:362-368 (1992); Henthorn	immune response. Additional
		<del> </del>	et al., Proc Natl Acad Sci USA	highly preferred indications
	<del></del>		85:6342-6346 (1988); Benson	include inflammation and
		_	et al., J Immunol 153(9):3862-	inflammatory disorders, and
	<del></del> ,		3873 (1994); and Black et al.,	treating joint damage in
			Virus Genes 12(2):105-117	patients with rheumatoid
			(1997), the content of each of	arthritis. An additional highly
		-	which are herein incorporated	preferred indication is sepsis.
			by reference in its entirety. T	Highly preferred indications
	<del></del>		cells that may be used	include neoplastic diseases
			according to these assays are	(e.g., leukemia, lymphoma,
			publicly available (e.g.,	and/or as described below
			through the ATCC).	under "Hyperproliferative
			Exemplary T cells that may be	Disorders"). Additionally,
			used according to these assays	highly preferred indications
			include the NK-YT cell line,	include neoplasms and
			 which is a human natural killer	cancers, such as, for example,
		-	cell line with cytolytic and	leukemia, lymphoma,
			cytotoxic activity.	melanoma, glioma (e.g.,

					is infection (e.g., an infectious
					disease as described below
	HCITHK65	1039	A activities A		under "Infectious Disease").
6	TICOLINO	1038	Activation of	Assays for the activation of	A preferred embodiment of
90			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
	T.		response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
	***			the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
		~~		transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
		- N-2		disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and
				Malm, Methods in Enzymol	suppressing a T cell-mediated
				216:362-368 (1992); Henthorn	immune response. Additional

highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid	arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and cancers, such as, for example.	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,
et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117	(1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g., through the ATCC).	used according to these assays include the NK-YT cell line, which is a human natural killer	cell line with cytolytic and cytotoxic activity.			

					leukopenia, thrombocytopenia.
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
	-				myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
	-				disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
		-	****		suppression of immune
					reactions to transplanted
		***			organs and tissues, hemophilia,
					hypercoagulation, diabetes
	-				mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
	201 m 1011				under "Infectious Disease").
5	HCUIM65	1039	Regulation of	Assays for the regulation of	A highly preferred indication
91			transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic
				polypeptides of the invention	retinopathy, diabetic
	1=			(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to activate the	nephropathy and/or other

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diseases and disorders as	Disorders" section below).	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the
DMEF1 response element in a	containing the GLUT4	promoter) and to regulate	insulin production. The	DMEF1 response element is	present in the GLUT4	promoter and binds to MEF2	transcription factor and another	transcription factor that is	required for insulin regulation	of Glut4 expression in skeletal	muscle. GLUT4 is the primary	insulin-responsive glucose	transporter in fat and muscle	tissue. Exemplary assays that	may be used or routinely	modified to test for DMEF1	response element activity (in	adipocytes and pre-adipocytes)	by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed inThai, M.V., et al., J	Biol Chem, 273(23):14285-92	(1998); Mora, S., et al., J Biol	Chem, 275(21):16323-8	(2000); Liu, M.L., et al., J Biol	Chem, 269(45):28514-21	(1994); "Identification of a 30-
											<b>****</b>																		
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"Infectious Diseases" section below, especially of the urinary tract and skin). An additional highly preferred	indication is obesity and/or complications associated with obesity. Additional highly	preferred indications include weight loss or alternatively, weight gain. Additional highly	preferred indications are complications associated with insulin resistance.							
base pair regulatory element and novel DNA binding protein that regulates the human GLUTA promoter in	transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10	(1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the	contents of each of which is herein incorporated by reference in its entirety.	Adipocytes and pre-adipocytes that may be used according to	these assays are publicly available (e.g., through the ATCC) and/or may be	routinely generated.  Exemplary cells that may be	used according to these assays include the mouse 3T3-L1 cell line which is an adherent	mouse preadipocyte cell line. Mouse 3T3-L1 cells are a	continuous substrain of 313 fibroblasts developed through clonal isolation. These cells	undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation

				culture conditions.	
Č	HCUIM65	1039	Activation of	Assays for the activation of	A highly preferred indication
91			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
			2.11	functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
			-	adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
	•			transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
				transcription through the	nonketotic hyperglycemic-
				cAMP response element that	hyperosmolar coma,
				may be used or routinely	cardiovascular disease (e.g.,

	modified to test cAMP-	heart disease, atherosclerosis,
	response element activity of	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
 	agonists or antagonists of the	described in the
 	invention) include assays	"Cardiovascular Disorders"
	disclosed in Berger et al., Gene	section below), dyslipidemia,
	66:1-10 (1998); Cullen and	endocrine disorders (as
	Malm, Methods in Enzymol	described in the "Endocrine
	216:362-368 (1992); Henthorn	Disorders" section below),
	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	et al., Mol Cell Biol	blindness), ulcers and impaired
	20(3):1008-1020 (2000); and	wound healing, and infection
	Klemm et al., J Biol Chem	(e.g., infectious diseases and
	273:917-923 (1998), the	disorders as described in the
	contents of each of which are	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety. Pre-	urinary tract and skin), carpal
	adipocytes that may be used	tunnel syndrome and
	according to these assays are	Dupuytren's contracture).
	publicly available (e.g.,	Additional highly preferred
	through the ATCC) and/or	indications are complications
 	may be routinely generated.	associated with insulin
 	Exemplary mouse adipocyte	resistance.
	cells that may be used	
	according to these assays	
	include 3T3-L1 cells. 3T3-L1	
	is an adherent mouse	
	preadipocyte cell line that is a	
	continuous substrain of 3T3	

				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
-	HCUIM65	1039	Activation of	Assays for the activation of	A highly preferred indication
16			transcription	transcription through the	is obesity and/or complications
			through serum	Serum Response Element	associated with obesity.
			response element in	(SRE) are well-known in the	Additional highly preferred
			pre-adipocytes.	art and may be used or	indications include weight loss
				routinely modified to assess	or alternatively, weight gain.
				the ability of polypeptides of	An additional highly preferred
				the invention (including	indication is diabetes mellitus.
				antibodies and agonists or	An additional highly preferred
				antagonists of the invention) to	indication is a complication
				regulate the serum response	associated with diabetes (e.g.,
				factors and modulate the	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in growth. Exemplary assays	(e.g., renal failure,
				for transcription through the	nephropathy and/or other
				SRE that may be used or	diseases and disorders as
				routinely modified to test SRE	described in the "Renal
				activity of the polypeptides of	Disorders" section below),
				the invention (including	diabetic neuropathy, nerve
				antibodies and agonists or	disease and nerve damage
				antagonists of the invention)	(e.g., due to diabetic
				include assays disclosed in	neuropathy), blood vessel
				Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
				(1998); Cullen and Malm,	impotence (e.g., due to diabetic
		į		Methods in Enzymol 216:362-	neuropathy or blood vessel

				368 (1992); Henthorn et al.,	blockage), seizures, mental
				Proc Natl Acad Sci USA	confusion, drowsiness,
				85:6342-6346 (1988); and	nonketotic hyperglycemic-
				Black et al., Virus Genes	hyperosmolar coma,
				12(2):105-117 (1997), the	cardiovascular disease (e.g.,
				content of each of which are	heart disease, atherosclerosis,
				herein incorporated by	microvascular disease,
				reference in its entirety. Pre-	hypertension, stroke, and other
				adipocytes that may be used	diseases and disorders as
				according to these assays are	described in the
				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslipidemia,
				may be routinely generated.	endocrine disorders (as
-				Exemplary mouse adipocyte	described in the "Endocrine
				cells that may be used	Disorders" section below),
				according to these assays	neuropathy, vision impairment
				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
				is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
				continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
				conditions known in the art.	insulin resistance.
,	HCUIM65	1039	Inhibition of	Reporter Assay: construct	
16			squalene synthetase	contains regulatory and coding	
			gene transcription.	sequence of squalene	
				synthetase, the first specific	
				enzyme in the cholesterol	

			·	biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its	
91	HCUIM65	1039	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic

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	Extracellular factors can cause	neuropathy), blood vessel
	an influx of calcium, leading to	blockage, heart disease, stroke,
	activation of calcium	impotence (e.g., due to diabetic
	responsive signaling pathways	neuropathy or blood vessel
	and alterations in cell	blockage), seizures, mental
	functions. Exemplary assays	confusion, drowsiness,
	that may be used or routinely	nonketotic hyperglycemic-
	modified to measure calcium	hyperosmolar coma,
	flux by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
· ·	the invention) include assays	hypertension, stroke, and other
	disclosed in: Satin LS, et al.,	diseases and disorders as
	Endocrinology, 136(10):4589-	described in the
	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
	(1995); Richardson SB, et al.,	endocrine disorders (as
	Biochem J, 288 ( Pt 3):847-51	described in the "Endocrine
	(1992); and, Meats, JE, et al.,	Disorders" section below),
	Cell Calcium 1989 Nov-	neuropathy, vision impairment
	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
	contents of each of which is	blindness), ulcers and impaired
	herein incorporated by	wound healing, and infection
	reference in its entirety.	(e.g., infectious diseases and
	Pancreatic cells that may be	disorders as described in the
	used according to these assays	"Infectious Diseases" section
	are publicly available (e.g.,	below, especially of the
	through the ATCC) and/or	urinary tract and skin), carpal
	may be routinely generated.	tunnel syndrome and
	Exemplary pancreatic cells that	
	may be used according to these	An additional highly preferred

	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-
	assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess
		Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
,		1039
		HCUIM65
		91

		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
-		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
	manda Sarama	216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
_		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
20.7		Henderson et al., Mol Cell Biol   (ALL), plasmacytomas,	(ALL), plasmacytomas,

				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
		-		blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HCUIM65	1039	Activation of	This reporter assay measures	Highly preferred indications
91			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-

nsed or r	used or routinely modified to	Related Disorders", and/or
assess th	assess the ability of	"Cardiovascular Disorders").
polypept	polypeptides of the invention	Preferred indications include
(includir	(including antibodies and	autoimmune diseases (e.g.,
agonists	agonists or antagonists of the	rheumatoid arthritis, systemic
invention	invention) to regulate NFAT	lupus erythematosis, multiple
transcrip	transcription factors and	sclerosis and/or as described
modulate	modulate expression of genes	below) and
involved in	l in	immunodeficiencies (e.g., as
ounumi	immunomodulatory functions.	described below). Preferred
Exempla	Exemplary assays for	indications include neoplastic
transcrip	transcription through the	diseases (e.g., leukemia,
NFAT re	NFAT response element that	lymphoma, melanoma,
may be u	may be used or routinely	prostate, breast, lung, colon,
modified	modified to test NFAT-	pancreatic, esophageal,
response	response element activity of	stomach, brain, liver, and
polypept	polypeptides of the invention	urinary tract cancers and/or as
(includin	(including antibodies and	described below under
agonists	agonists or antagonists of the	"Hyperproliferative
invention	invention) include assays	Disorders"). Other preferred
disclosed	disclosed in Berger et al., Gene	indications include benign
66:1-10	66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, M	Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Pr	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-	85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):12	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	mmunol	leukemias, Hodgkin's disease,
165(12):	165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchins	Hutchinson and McCloskey, J	(ALL), plasmacytomas,

				Biol Chem 270(27):16333-	multiple myeloma. Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS.
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
_				these assays include the HMC-	•
-				1 cell line, which is an	
-			-	immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
-				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HCUIM65	1039	Activation of	This reporter assay measures	Highly preferred indication
191			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in HMC-1	rhinitis. Additional highly
			response element in	human mast cell line.	preferred indications include
			immune cells (such	Activation of NFkB in mast	infection (e.g., an infectious
			as mast cells).	cells has been linked to	disease as described below
		_		production of certain	under "Infectious Disease"),
				cytokines, such as IL-6 and IL-	and inflammation and
				9. Assays for the activation of	inflammatory disorders.
				transcription through the	Preferred indications include
				NFKB response element are	immunological and

	rders (e.g.,	under	and	orders").	s also	diseases	hritis,	nematosis,	ıd/or as	þ	(e.g., as	referred	nde	e.g.,	a,	s described		•	pa.	reoplasms	for	lymphoma,	tate,	oancreatic,	ı, brain,	ancers and	ınder	_		-	
	hempatopoietic disorders (e.g.,	as described below under	"Immune Activity", and	"Blood-Related Disorders").	Preferred indications also	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".		
ŀ		as de	ımI,,	"Blo	Pref	inclu	(e.g.	syste	mult	desc	imm	desc	indic	neop	lenke	mela	belo	"Hy	Diso	indic		exan						"Hy			
	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Stassen	et al, J Immunol 166(7):4391-8	(2001); and Marquardt and	Walker, J Allergy Clin	Immunol 105(3):500-5 (2000),	
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	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and e cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders".
are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1039
	HCUIM65
	91

				vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
			-	vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
м				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
				endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
				expression of VCAM	benign dysproliferative
	,			(CD106), a membrane-	disorders and pre-neoplastic
	,			associated protein, can be	conditions, such as, for
				upregulated by cytokines or	example, hyperplasia,
				other factors, and contributes	metaplasia, and/or dysplasia.
				to the extravasation of	
	-			lymphocytes, leucocytes and	
				other immune cells from blood	
				vessels; thus VCAM	
				expression plays a role in	
				promoting immune and	
1				inflammatory responses.	
	HCUIM65	1039	Activation of	Assays for the activation of	Highly preferred indications
91			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications

		of polypeptides of the	include autoimmune diseases
		invention (including antibodies	(e.g., rheumatoid arthritis,
		and agonists or antagonists of	systemic lupus erythematosis,
		the invention) to regulate	multiple sclerosis and/or as
		NFAT transcription factors and	described below),
		modulate expression of genes	immunodeficiencies (e.g., as
		involved in	described below), boosting a T
		immunomodulatory functions.	cell-mediated immune
		Exemplary assays for	response, and suppressing a T
		transcription through the	cell-mediated immune
		NFAT response element that	response. Additional highly
		may be used or routinely	preferred indications include
		modified to test NFAT-	inflammation and
		response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
	-	agonists or antagonists of the	infectious disease as described
		invention) include assays	below under "Infectious
		disclosed in Berger et al., Gene	Disease"). Preferred
	-	66:1-10 (1998); Cullen and	indications include neoplastic
		Malm, Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988);	"Hyperproliferative
		Aramburu et al., J Exp Med	Disorders"). Preferred
_		182(3):801-810 (1995); De	indications include neoplasms
		Boer et al., Int J Biochem Cell	and cancers, such as, for
		Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
		Fraser et al., Eur J Immunol	and prostate, breast, lung,
		29(3):838-844 (1999); and	colon, pancreatic, esophageal,
		Yeseen et al., J Biol Chem	stomach, brain, liver and

				268(19):14285-14293 (1993).	urinary cancer. Other preferred
				the contents of each of which	indications include benign
				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. NK	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human NK cells	leukopenia, thrombocytopenia,
	,			that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
			-		disease, sepsis, neutropenia,
. 10					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HCUIM65	1039	Activation of	Assays for the activation of	Highly preferred indications
91			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as natural killer	to assess the ability of	as described below under
			cells).	polypeptides of the invention	"Immune Activity", "Blood-

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Related Disorders", and/or "Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include
(including antibodies and agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	NK cells that may be used
				-			****							-												-			

				according to these assays are	benign dysproliferative
				through the ATCC).	conditions, such as, for
				Exemplary NK cells that may	example, hyperplasia,
				be used according to these	metaplasia, and/or dysplasia.
-				assays include the NK-YT cell	Preferred indications also
				line, which is a human natural	include anemia, pancytopenia,
				killer cell line with cytolytic	leukopenia, thrombocytopenia,
				and cytotoxic activity.	Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
				-	disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
				The state of the s	organs, asthma and allergy.
	HCUIM65	1039	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha

production. Preferred indications include blood disorders (e.g., as described	below under "Immune Activity", "Blood-Related	Disorders", and/or "Cardiovascular Disorders"),	Highly preferred indications	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative
antagonists of the invention) to regulate serum response factors and modulate the	expression of genes involved in growth and upregulate the	function of growth-related genes in many cell types.	Exemplary assays for transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).
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			Exemplary T cells that may be	Disorders"). Additionally.
			used according to these assays	highly preferred indications
			include the NK-YT cell line,	include neoplasms and
			which is a human natural killer	cancers, such as, for example,
			cell line with cytolytic and	leukemia, lymphoma,
			cytotoxic activity.	melanoma, glioma (e.g.,
				malignant glioma), solid
		<del></del>		tumors, and prostate, breast,
				lung, colon, pancreatic,
		•		esophageal, stomach, brain,
				liver and urinary cancer. Other
				preferred indications include
				benign dysproliferative
-				disorders and pre-neoplastic
				conditions, such as, for
		-		example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include
				anemia, pancytopenia,
	40-1-			leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
			•	plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
•				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues, hemophilia,

	and agonists or antagonists of the invention) include assays	metaplasia, and/or dysplasia. Preferred indications include
	 disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	autoimmune diseases (e.g., rheumatoid arthritis, systemic
	Malm, Methods in Enzymol	lupus erythematosis, multiple
	 216:362-368 (1992); Henthorn	sclerosis and/or as described
	et al., Proc Natl Acad Sci USA	below), immunodeficiencies
-	 85:6342-6346 (1988);	(e.g., as described below),
	Matikainen et al., Blood	boosting a T cell-mediated
	 93(6):1980-1991 (1999); and	immune response, and
	Henttinen et al., J Immunol	suppressing a T cell-mediated
	155(10):4582-4587 (1995), the	immune response. Additional
	 contents of each of which are	preferred indications include
	herein incorporated by	inflammation and
-	reference in its entirety.	inflammatory disorders.
	Exemplary human T cells,	Highly preferred indications
	such as the SUPT cell line, that	include blood disorders (e.g.,
	may be used according to these	as described below under
	assays are publicly available	"Immune Activity", "Blood-
	 (e.g., through the ATCC).	Related Disorders", and/or
		"Cardiovascular Disorders"),
		and infection (e.g., viral
		infections, tuberculosis,
		infections associated with
		chronic granulomatosus
		disease and malignant
		osteoporosis, and/or an
		infectious disease as described
		below under "Infectious
		Disease"). An additional
		preferred indication is

idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as
	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes
	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).
	1040
	HCWEB58
·	92

	involved in	described below) boosting a T
	immunomodulatory functions.	cell-mediated immune
	Exemplary assays for	response, and suppressing a T
	transcription through the	cell-mediated immune
	NFAT response element that	response. Additional highly
	may be used or routinely	preferred indications include
	modified to test NFAT-	inflammation and
	response element activity of	inflammatory disorders. An
	polypeptides of the invention	additional highly preferred
	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988);	"Hyperproliferative
	Aramburu et al., J Exp Med	Disorders"). Preferred
	182(3):801-810 (1995); De	indications include neoplasms
	Boer et al., Int J Biochem Cell	and cancers, such as, for
	Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. NK	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,
	according to these assays are	metaplasia, and/or dysplasia.

				publicly available (e.g.,	Preferred indications also
				through the AICC).	include anemia, pancytopenia,
				Exemplary human NK cells	leukopenia, thrombocytopenia,
_	waa 12			that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
	-				disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
				10 to	asthma and allergy.
	HCWGU37	1041	Calcium flux in	Assays for measuring calcium	Preferred embodiments of the
			chondrocytes	flux are well-known in the art	invention include using
_				and may be used or routinely	polypeptides of the invention
				modified to assess the ability	(or antibodies, agonists, or
				of polypeptides of the	antagonists thereof) in
				invention (including antibodies	detection, diagnosis,
				and agonists or antagonists of	prevention, and/or treatment of
				the invention) to mobilize	Bone and Cartilage Diseases,
				calcium. Cells normally have	including but not limited to
				very low concentrations of	Arthritis, Cartilige repair, Bone
				cytosolic calcium compared to	Repair, Osteoporosis, and
				much higher extracellular	related tumors including
				calcium. Extracellular factors	chondrosarcomas,

ium, chondroblastomas, and	chondromas.	gu	T.			sure	tes		es,	ırtz		ətti				33	hof	pa			re					ays	es.	f A highly preferred indication	is diabetes mellitus.	
can cause an influx of calcium,	leading to activation of	calcium responsive signaling	pathways and alterations in	cell functions. Exemplary	assays that may be used or	routinely modified to measure	calcium flux in chondrocytes	include assays disclosed in:	Asada S, et al., Inflamm Res,	50(1):19-23 (2001); Schwartz	Z, et al., J Bone Miner Res,	6(7):709-718 (1991); Iannotti	JP, et al., J Bone Joint Surg	Am, 67(1): 113-120 (1985);	Sullivan E., et al., Methods	Mol Biol 1999; 114:125-133	(1999), the contents of each of	which is herein incorporated	by reference in its entirety.	Cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary cells that may be	used according to these assays	include bovine chondrocytes.	Assays for the regulation of	transcription through the	DMEF1 response element are
	•																											Regulation of	transcription via	DMEF1 response
			_		<u>.</u>												•											1042		
																												HCWKC15		
																													94	

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adipocytes and
aupocytes

disclosed in Thai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound bealing, and infection
Chem, 269(45):28514-21 (1994); "Identification of a 30- base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in	(e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin). An additional highly preferred
transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly
herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be	preserved indications are complications associated with insulin resistance.
Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line.	

				Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3	
				fibroblasts developed through	
				clonal isolation. These cells	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
		- 1860 ·		appropriate differentiation	
	HCWKC15	1042	Activation of	A score for the estimation of	A 1-1-1-
0	CIONINOII	7101	ACUVALIOII OI	Assays for tile activation of	A nigniy preferred indication
<del>,</del> 74			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
		- 1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1	adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
		•		invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
-				3T3-L1/CRE reporter assay	diseases and disorders as
	-			may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
			-	adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,

binding sequence for the	impotence (e.g due to diahetic
transcription factor CREB	neuropathy or blood vessel
(CRE binding protein).	blockage), seizures, mental
 Exemplary assays for	confusion, drowsiness,
transcription through the	nonketotic hyperglycemic-
cAMP response element that	hyperosmolar coma,
may be used or routinely	cardiovascular disease (e.g.,
modified to test cAMP-	heart disease, atherosclerosis,
response element activity of	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in Berger et al., Gene	le section below), dyslipidemia,
 66:1-10 (1998); Cullen and	endocrine disorders (as
Malm, Methods in Enzymol	described in the "Endocrine
   216:362-368 (1992); Henthorn	
et al., Proc Natl Acad Sci USA	_
 85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
et al., Mol Cell Biol	blindness), ulcers and impaired
20(3):1008-1020 (2000); and	wound healing, and infection
Klemm et al., J Biol Chem	(e.g., infectious diseases and
273:917-923 (1998), the	disorders as described in the
contents of each of which are	"Infectious Diseases" section
herein incorporated by	below, especially of the
reference in its entirety. Pre-	urinary tract and skin), carpal
adipocytes that may be used	tunnel syndrome and
according to these assays are	Dupuytren's contracture).
publicly available (e.g.,	Additional highly preferred
through the ATCC) and/or	indications are complications
may be routinely generated.	associated with insulin

resistance.	A highly preferred indication is obesity and/or complications associated with obesity.  Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal
Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE positivity of the molynomical and antity of the molynomical antity of the molyn
	Activation of transcription through serum response element in pre-adipocytes.
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diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below). Additional highly	preferred indications are
the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under
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				appropriate differentiation	complications associated with
	HCWKC15	1042	Activation of	Assays for the activation of	Highly preferred indications
94			transcription	transcription through the	include asthma, allergy,
			through GAS	Gamma Interferon Activation	hypersensitivity reactions,
			response element in	Site (GAS) response element	inflammation, and
			immune cells (such	are well-known in the art and	inflammatory disorders.
		ú.	as eosinophils).	may be used or routinely	Additional highly preferred
				modified to assess the ability	indications include immune
	-			of polypeptides of the	and hematopoietic disorders
				invention (including antibodies	(e.g., as described below under
		-		and agonists or antagonists of	"Immune Activity", and
				the invention) to modulate	"Blood-Related Disorders"),
<u>.</u>				gene expression (commonly	autoimmune diseases (e.g.,
				via STAT transcription factors)	rheumatoid arthritis, systemic
000				involved in a wide variety of	lupus erythematosis, Crohn"s
	-			cell functions. Exemplary	disease, multiple sclerosis
				assays for transcription	and/or as described below),
				through the GAS response	immunodeficiencies (e.g., as
				element that may be used or	described below), boosting an
			-	routinely modified to test	eosinophil-mediated immune
				GAS-response element activity	response and, alternatively,
				of polypeptides of the	suppressing an eosinophil-
				invention (including antibodies	mediated immune response.
				and agonists or antagonists of	
-				the invention) include assays	
				disclosed in Berger et al., Gene	
				66:1-10 (1998); Cullen and	
				Malm, Methods in Enzymol	
		-		216:362-368 (1992); Henthorn	
				et al., Proc Natl Acad Sci USA	

85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to activate or	inhibit activation of immune	cells include assays disclosed	and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL
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	Highly preferred indications include asthma, allergy, hypersensitivity reactions, and inflammation. Preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"),
adapter in interleukin-5 signaling in eosinophils" J Biol Chem; Oct 20;275(42):33167-75 (2000); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	Activation of transcription through NFKB response element in immune cells (such as EOL1 cells).
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		agonists or antagonists of the	immunological disorders.
		invention) to regulate NFKB	inflammation and
		transcription factors and	inflammatory disorders (e.g.,
		modulate expression of	as described below under
		immunomodulatory genes.	"Immune Activity", and
		Exemplary assays for	"Blood-Related Disorders").
	***	transcription through the	Preferred indications include
		NFKB response element that	autoimmune diseases (e.g.,
		may be used or rountinely	rheumatoid arthritis, systemic
		modified to test NFKB-	lupus erythematosis, multiple
		response element activity of	sclerosis and/or as described
		polypeptides of the invention	below) and
		(including antibodies and	immunodeficiencies (e.g., as
71-		agonists or antagonists of the	described below).
		invention) include assays	
		disclosed in Berger et al., Gene	
		66:1-10 (1998); Cullen and	
		Malm, Methods in Enzymol	
		216:362-368 (1992); Henthorn	
		et al., Proc Natl Acad Sci USA	
		85:6342-6346 (1988); Valle	
		Blazquez et al, Immunology	
		90(3):455-460 (1997);	
		Aramburau et al., J Exp Med	
		82(3):801-810 (1995); and	
		Fraser et al., 29(3):838-844	
		(1999), the contents of each of	
		which are herein incorporated	
		by reference in its entirety.	
	_	For example, a reporter assay	
		(which measures increases in	

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	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also
transcription inducible from a NFkB responsive element in EOL-1 cells) may link the NFKB element to a repeorter gene and binds to the NFKB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well brown in the
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
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		art and may be used or	as described below under
		routinely modified to assess	"Immune Activity", "Blood-
		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
•		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
-		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
-		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	7 777	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,

				Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol	acute lymphocytic anemia (ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
•	HCWKC15	1042	Activation of	This reporter assay measures	Highly preferred indications
94			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
	district the second sec			Activated T cells (NFAT)	include blood disorders (e.g.,

response element are well-	as described below under
known in the art and may be	"Immune Activity", "Blood-
used or routinely modified to	Related Disorders", and/or
assess the ability of	"Cardiovascular Disorders").
polypeptides of the invention	Preferred indications include
(including antibodies and	autoimmune diseases (e.g.,
agonists or antagonists of the	rheumatoid arthritis, systemic
invention) to regulate NFAT	lupus erythematosis, multiple
 transcription factors and	sclerosis and/or as described
modulate expression of genes	below) and
involved in	immunodeficiencies (e.g., as
immunomodulatory functions.	described below). Preferred
 Exemplary assays for	indications include neoplastic
transcription through the	diseases (e.g., leukemia,
NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
(including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
 invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
 85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
 et al., J Immunol	leukemias, Hodgkin's disease,

				165(12):7215-7223 (2000);	acute lymphocytic anemia
				Hutchinson and McCloskey, J	(ALL), plasmacytomas,
			-	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
-				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
•				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
•				through the ATCC).	hypercoagulation, diabetes
	-			Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HCWKC15	1042	Activation of	This reporter assay measures	Highly preferred indication
94			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in HMC-1	rhinitis. Additional highly
			response element in	human mast cell line.	preferred indications include
			immune cells (such	Activation of NFkB in mast	infection (e.g., an infectious
			as mast cells).	cells has been linked to	disease as described below
				production of certain	under "Infectious Disease"),
				cytokines, such as IL-6 and IL-	and inflammation and
				9. Assays for the activation of	inflammatory disorders.

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Preferred indications include	immunological and	hempatopoietic disorders (e.g.,	as described below under	"Immune Activity", and	"Blood-Related Disorders").	Preferred indications also	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".
transcription through the	NFKB response element are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Stassen	et al, J Immunol 166(7):4391-8	(2001); and Marquardt and	Walker, J Allergy Clin
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	Highly preferred indications include allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include hematopoietic and immunological disorders (e.g., as described below under
Immunol 105(3):500-5 (2000), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element in immune cells (such as in the human HMC-1 mast cell line) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of
	Activation of transcription through STAT6 response element in immune cells (such as mast cells).
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1	the invention) to regulate	"Immune Activity", "Blood-
	STAT6 transcription factors	Related Disorders", and/or
	and modulate the expression of	"Cardiovascular Disorders"),
	multiple genes. Exemplary	autoimmune diseases (e.g.,
	assays for transcription	rheumatoid arthritis, systemic
	through the STAT6 response	lupus erythematosis, multiple
	element that may be used or	sclerosis and/or as described
	routinely modified to test	below), and
	STAT6 response element	immunodeficiencies (e.g., as
 	activity of the polypeptides of	described below). Preferred
	the invention (including	indications include neoplastic
	antibodies and agonists or	diseases (e.g., leukemia,
	antagonists of the invention)	lymphoma, melanoma, and/or
	include assays disclosed in	as described below under
	Berger et al., Gene 66:1-10	"Hyperproliferative
	(1998); Cullen and Malm,	Disorders"). Preferred
	Methods in Enzymol 216:362-	indications include neoplasms
	368 (1992); Henthorn et al.,	and cancer, such as, for
	Proc Natl Acad Sci USA	example, leukemia, lymphoma,
	85:6342-6346 (1988);	melanoma, and prostate,
	Sherman, Immunol Rev	breast, lung, colon, pancreatic,
	179:48-56 (2001); Malaviya	esophageal, stomach, brain,
	and Uckun, J Immunol	liver and urinary cancer. Other
	168:421-426 (2002); Masuda	preferred indications include
	et al., J Biol Chem	benign dysproliferative
	275(38):29331-29337 (2000);	disorders and pre-neoplastic
	and Masuda et al., J Biol Chem	conditions, such as, for
	276:26107-26113 (2001), the	example, hyperplasia,
	contents of each of which are	metaplasia, and/or dysplasia.
	herein incorporated by	Preferred indications include
I	reference in its entirety. Mast	hematopoietic and

immunological disorders such as arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications include immunological and hempatopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"). Preferred indications also
cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an	immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of
		Activation of transcription through NFKB response element in immune cells (such as basophils).
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(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".								
Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Basophils that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous
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			1 (100)	leukemia. It is an immature	
	<u></u>			prebasophilic cell line that can	
				be induced to differentiate into	
				mature basophils.	
. ,	HCWKC15	1042	Activation of	Assays for the activation of	Highly preferred indications
94			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
	-			Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred
				66:1-10 (1998); Cullen and	indications include neoplastic

diseases (e.g., leukemia, lymphoma, and/or as described below under	"Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for	example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993).	the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are	publicly available (e.g., through the ATCC).  Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with	cytolytic and cytotoxic activity.
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					hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and alleroy
76	HCWKC15	1042	Activation of transcription through NFKB response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases
	78.0			00:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	(e.g., melanoma, leukemia, lymphoma, and/or as described below under

		et al Proc Natl Acad Sci USA	"Hynemroliferative
		85.6342-6346 (1988)· Valle	Disorders") Highly preferred
		Blazonez et al Imminology	indications include noculous
		90(3):455-460 (1997):	mulcations include iteopiasins
		Aramburan et al J Exp Med	example melanoma renal cell
		82(3):801-810 (1995); and	carcinoma, leukemia,
		Fraser et al., 29(3):838-844	lymphoma, and prostate,
		(1999), the contents of each of	breast, lung, colon, pancreatic,
		which are herein incorporated	esophageal, stomach, brain,
	-	by reference in its entirety.	liver and urinary cancer. Other
		NK cells that may be used	preferred indications include
		according to these assays are	benign dysproliferative
		publicly available (e.g.,	disorders and pre-neoplastic
		through the ATCC).	conditions, such as, for
		Exemplary NK cells that may	example, hyperplasia,
		be used according to these	metaplasia, and/or dysplasia.
		assays include the NK-YT cell	Preferred indications also
		line, which is a human natural	include anemia, pancytopenia,
		killer cell line with cytolytic	leukopenia, thrombocytopenia,
		and cytotoxic activity.	Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, sepsis, neutropenia,
			neutrophilia, psoriasis,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
			meningitis, Lyme Disease,
-			suppression of immune

					reactions to transplanted
	HCWKC15	1042	Activation of	A activition of the of	organs, astrima and allergy.
76		7101	tacuration of	Assays for the activation of	A preferred embodiment of
+ (			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
			-	antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and
				Malm, Methods in Enzymol	suppressing a T cell-mediated
,				216:362-368 (1992); Henthorn	immune response. Additional
				et al., Proc Natl Acad Sci USA	highly preferred indications

	85:6342-6346 (1988); Benson	include inflammation and
	 et al., J Immunol 153(9):3862-	inflammatory disorders, and
	3873 (1994); and Black et al.,	treating joint damage in
	 Virus Genes 12(2):105-117	patients with rheumatoid
	(1997), the content of each of	arthritis. An additional highly
	which are herein incorporated	preferred indication is sepsis.
	by reference in its entirety. T	Highly preferred indications
	cells that may be used	include neoplastic diseases
	 according to these assays are	(e.g., leukemia, lymphoma,
	 publicly available (e.g.,	and/or as described below
	through the ATCC).	under "Hyperproliferative
	Exemplary T cells that may be	Disorders"). Additionally,
_	used according to these assays	highly preferred indications
	include the NK-YT cell line,	include neoplasms and
_	 which is a human natural killer	cancers, such as, for example,
	cell line with cytolytic and	leukemia, lymphoma,
	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
<u>u</u>		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,

					Hodgkin's disease, acute
	-				lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
-					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
	. 1	-			cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
2	HCWKCIS	1042	Activation of	Assays for the activation of	Highly preferred indications
<del>,</del>	-		transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as natural killer	to assess the ability of	as described below under
			cells).	polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases

modulate expression of	(e.g., rheumatoid arthritis,
immunomodulatory genes.	systemic lupus erythematosis,
 Exemplary assays for	multiple sclerosis and/or as
transcription through the	described below), and
NFKB response element that	immunodeficiencies (e.g., as
may be used or rountinely	described below). An
modified to test NFKB-	additional highly preferred
response element activity of	indication is infection (e.g.,
polypeptides of the invention	AIDS, and/or an infectious
 (including antibodies and	disease as described below
agonists or antagonists of the	under "Infectious Disease").
invention) include assays	Highly preferred indications
 disclosed in Berger et al., Gene	include neoplastic diseases
66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
Malm, Methods in Enzymol	lymphoma, and/or as described
216:362-368 (1992); Henthorn	below under
 et al., Proc Natl Acad Sci USA	"Hyperproliferative
85:6342-6346 (1988); Valle	Disorders"). Highly preferred
Blazquez et al, Immunology	indications include neoplasms
90(3):455-460 (1997);	and cancers, such as, for
Aramburau et al., J Exp Med	example, melanoma, renal cell
82(3):801-810 (1995); and	carcinoma, leukemia,
Fraser et al., 29(3):838-844	lymphoma, and prostate,
(1999), the contents of each of	breast, lung, colon, pancreatic,
which are herein incorporated	esophageal, stomach, brain,
by reference in its entirety.	liver and urinary cancer. Other
NK cells that may be used	preferred indications include
according to these assays are	benign dysproliferative
 publicly available (e.g.,	disorders and pre-neoplastic
through the ATCC).	conditions, such as, for
Exemplary human NK cells	example, hyperplasia,

				cell line	arthritis asthma AIDS
					allergy, anemia, pancytopenia.
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression of
					immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HCWKC15	1042	Activation of	Assays for the activation of	A highly preferred
94			transcription	transcription through the CD28	embodiment of the invention
		41	through CD28	response element are well-	includes a method for
			response element in	known in the art and may be	stimulating T cell proliferation.
			immune cells (such	used or routinely modified to	An alternative highly preferred
			as T-cells).	assess the ability of	embodiment of the invention
				polypeptides of the invention	includes a method for
-				(including antibodies and	inhibiting T cell proliferation.
		3.		agonists or antagonists of the	A highly preferred
				invention) to stimulate IL-2	embodiment of the invention
				expression in T cells.	includes a method for
				Exemplary assays for	activating T cells. An
				transcription through the CD28	alternative highly preferred
				response element that may be	embodiment of the invention
		10.2		used or routinely modified to	includes a method for
				test CD28-response element	inhibiting the activation of
				activity of polypeptides of the	and/or inactivating T cells.

	vention	•	reasing)	alternative	odiment	des a	(e.g.,	ction.	ferred			Yrs.	cations	diseases	ıritis,	ematosis,	1/or as		(e.g., as	osting a T	<u>ie</u>	ssing a T	le	referred	eoplastic	oma, renal	mia,	described		
A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	IL-2 production. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting (e.g.,	reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Highly preferred	indications include neoplastic	diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described	below under	"Hypernroliferative
A high	empod	includ	stimul	IL-2 p	highly	of the	metho	reduci	Addit	indica	inflan	inflan	High	includ	(e.g.,	syster	multip	descri	immu	descri	cell-n	respoi	cell-n	respoi	indica	diseas	cell c	lympl	below	u.H.,
invention (including antihodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.			

Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal	cell carcinoma (e.g., metastatic	renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma), and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	A highly preferred indication	includes infection (e.g.,	AIDS, tuberculosis, infections	associated with granulomatous	disease, and osteoporosis,	and/or as described below	under "Infectious Disease"). A	highly preferred indication is	AIDS. Additional highly	preferred indications include	suppression of immune	reactions to transplanted	organs and/or tissues, uveitis,
				_					-			- Total																		
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																		-				-								

					psoriasis, and tropical spastic
					paranaresis Preferred
					nch
					disorders (e.g., as described
					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications also
					include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, granulomatous
					disease, inflammatory bowel
				(	disease, sepsis, neutropenia,
					neutrophilia, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HCWKC15	1042	Activation of	Assays for the activation of	Highly preferred indications
94			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for

example, leukemia, lymphoma	(e.g., 1 cell lymphoma, Burkitt's lymphoma non-	Hodgkins lymphoma,	Hodgkin"s disease),	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,
invention (including antibodies	and agonists or antagonists of	STAT transcription factors and	modulate gene expression	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that
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										,																			

					asthma and allergy.
	HCWKC15	1042	Activation of	Assays for the activation of	Highly preferred indications
94			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as T-cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
		-		NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred
			-	66:1-10 (1998); Cullen and	indications include neoplastic
				Malm, Methods in Enzymol	diseases (e.g., leukemia,
				216:362-368 (1992); Henthorn	lymphoma, and/or as described
				et al., Proc Natl Acad Sci USA	below under

"Hyperproliferative Disorders"). Preferred indications include neoplasms	and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal,	stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and	as, for example, hyperplasia, metaplasia, and/or dysplasia.  Preferred indications also include anemia, pancytopenia,	Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous	disease, initialimatory bower disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,
85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer	Et al., Int J Blochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and	Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by	cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exempliary numan 1 cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	
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					asthma and allergy.
	HCWKC15	1042	Activation of	Assays for the activation of	Highly preferred indications
94			transcription	transcription inrough the	include initialination and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preterred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
_				NFKB response element that	immunodeficiencies (e.g., as
-				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
	-	•		216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative
		-44		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
				al., Virus Gnes 15(2):105-117	indications include neoplasms

		response element activity of	microvascular disease
	•	polypeptides of the invention	hypertension, stroke, and other
		(including antibodies and	diseases and disorders as
		agonists or antagonists of the	described in the
		invention) include assays	"Cardiovascular Disorders"
		disclosed in Berger et al., Gene	section below), dyslipidemia,
		66:1-10 (1998); Cullen and	endocrine disorders (as
		Malm, Methods in Enzymol	described in the "Endocrine
		216:362-368 (1992); Henthorn	Disorders" section below),
		et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
		85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
		et al., Mol Cell Biol	blindness), ulcers and impaired
		20(3):1008-1020 (2000); and	wound healing, and infection
		Klemm et al., J Biol Chem	(e.g., infectious diseases and
		273:917-923 (1998), the	disorders as described in the
		contents of each of which are	"Infectious Diseases" section
	4.0	herein incorporated by	below, especially of the
		reference in its entirety. Pre-	urinary tract and skin), carpal
		adipocytes that may be used	tunnel syndrome and
		according to these assays are	Dupuytren's contracture).
		publicly available (e.g.,	Additional highly preferred
-		through the ATCC) and/or	indications are complications
		may be routinely generated.	associated with insulin
		Exemplary mouse adipocyte	resistance.
		cells that may be used	
		according to these assays	
		include 3T3-L1 cells. 3T3-L1	
		is an adherent mouse	
		preadipocyte cell line that is a	
	and a second	continuous substrain of 3T3	
		fibroblast cells developed	

				through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	
95	HCWLD74	1043	Activation of transcription	This reporter assay measures activation of the GATA-3	Highly preferred indications include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and inflammation and
				activation of transcription	inflammatory disorders.
_				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,
				routinely modified to test	lymphoma, melanoma,

prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary tract cancers and/or as described below under	"Hyperproliferative Disorders"). Other preferred	indications include benign	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.	
GATA3-response element activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp Onant Biol 64:563-571 (1999):	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to	these assays include the HMC-	1 cell line, which is an	immature human mast cell line
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				established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	
95	HCWLD74	1043	Activation of transcription	This reporter assay measures activation of the NFAT	Highly preferred indications include allergy, asthma, and
			through NFAT response element in	signaling pathway in HMC-1 human mast cell line.	rhinitis. Additional preferred indications include infection
			immune cells (such	Activation of NFAT in mast cells has been linked to	(e.g., an infectious disease as described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
	-			through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
	,			transcription through the	diseases (e.g., leukemia,
				NFAT response element that	lymphoma, melanoma,

may be used or routinely	prostate, breast, lung, colon,
 modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
(including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
 invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
al., J Exp Med 188:527-537	granulomatous disease,
 (1998), the contents of each of	inflammatory bowel disease,
which are herein incorporated	sepsis, neutropenia,
by reference in its entirety.	neutrophilia, psoriasis,
Mast cells that may be used	suppression of immune
according to these assays are	reactions to transplanted
publicly available (e.g.,	organs and tissues, hemophilia,
through the ATCC).	hypercoagulation, diabetes
Exemplary human mast cells	mellitus, endocarditis,
that may be used according to	meningitis, and Lyme Disease.
these assays include the HMC-	

st cell line peripheral th mast thickits of	tion of Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-modified "Cardiovascular Disorders"), and infectious disease as described below under "Infectious below under "Infectious orintication indications include autoimmune diseases (e.g., involved indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), hoosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include	
I cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays
	Activation of transcription through cAMP response element in immune cells (such as T-cells).	
	HCWLD74 1043	
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Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below	Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate,	esophageal, stomach, brain, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia	AIDS, granulomatous disease, inflammatory bowel disease,
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci 11SA	85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665	which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are	through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the HT2 cell line, which is a suspension	culture of IL-2 dependent 1 cells that also respond to IL-4.	

					sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
95	HCWLD74	1043	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and
				response element activity of polypeptides of the invention	inflammatory disorders. An additional highly preferred

indication is infection (e.g., an infectious disease as described	below under "Infectious Disease"). Preferred	₽.	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel
(including antibodies and agonists or antagonists of the	invention) include assays disclosed in Berger et al Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Aramburu et al., J Exp Med	182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. NK	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NK-	YT cell line, which is a human	natural killer cell line with	cytolytic and cytotoxic	activity.
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						•		-				-									•							

disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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eficienc	l below)	mediate	, and	ell-medi	. Addit	ndicatio	tion and	orders, a	lage in	ımatoid	tional hi	on is sep	indicatic	c disease	/mphom	ed below	iferative	litionally	ndicatio	s and	for exan	oma,	a (e.g.,	), solid	ate, brea	reatic,	ach, bra	cancer.	ons incl	24.40
pounuu	escribed	a T cell-	esponse	ng a T c	esbouse	eferred i	ıflamma	tory dis	oint dam	vith rheu	An addi	indicati	eferred	eoplasti	cemia, ly	describe	yperprol	"). Add	eferred i	eoplasm	uch as,	, lympho	a, gliom	t glioma	nd prost	on, panc	al, stom	urinary	indicati	corrolife
below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	henian dysproliferative
itagonist	lude ass	er et al.,	Jullen an	n Enzyn	(2); Hen	cad Sci	88); Bei	153(9):3	Black et	):105-11	nt of eac	incorpor	entirety	nseq	e assays	(e.g.,	<u>(</u> )	s that ma	these as	T cell li	natural	lytic and								
ists or ar	tion) inc	in Berg	1998); C	ethods ii	368 (199	c Natl A	5346 (19	nmunol	94); and	nes 12(2	e conter	herein	nce in its	may be	to these	ıvailable	he ATC	y T cell	ording to	e NK-Y	a human	vith cytc	activity							
and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.							
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				disorders and pre-neoplastic conditions, such as, for
				example, hyperplasia, metaplasia, and/or dysplasia.
				Preferred indications include anemia, pancytopenia,
.,,,,				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
<u>.</u>				neutrophilia, psoriasis,
				suppression of immune
		•		reactions to transplanted
				organs and tissues, hemophilia,
				hypercoagulation, diabetes
				mellitus, endocarditis,
	-			meningitis, Lyme Disease,
	,_			cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
=	1043	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include neoplastic diseases
		through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
		response element in	Site (GAS) response element	and/or as described below

							_																							
under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma	(e.g., T cell lymphoma,	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin's disease),	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated		preferred indications include
are well-known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to regulate	STAT transcription factors and	modulate gene expression	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are
immune cells (such	as T-cells).																													
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pı	sorders.	l indications	sorders (e.g.,	ow under	ity", "Blood-	rs", and/or	· Disorders"),	.g., viral	culosis,	iated with	matosus	ignant	ıd/or an	se as described	nfections	additional	tion is	onary fibrosis.	utions include	openia,	leukopenia, thrombocytopenia,	tic anemia	ytomas,	ma, arthritis,	natous disease,	owel disease,	enia,	oriasis,	immune	nsplanted
inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thro	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted
herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).																								
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					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
96	HCWUM50	1044	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte
			, and the second second	assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin	activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the

	Dudominol Diobotos	activation of (e a decreasing)
	Elidocillioi Diancies	activation of (e.g., acticusing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
	 410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
 	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
 	reference in its entirety.	described below under
 	Mouse adipocyte cells that	"Hyperproliferative
	 may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
 	according to these assays	stroke, impotence and/or as
	include 3T3-L1 cells. 3T3-L1	described below under
	 is an adherent mouse	"Immune Activity",
	preadipocyte cell line that is a	"Cardiovascular Disorders",
	continuous substrain of 3T3	and/or "Blood-Related
	fibroblast cells developed	Disorders"), immune disorders
	through clonal isolation and	(e.g., as described below under
	undergo a pre-adipocyte to	"Immune Activity"), neural
 	adipose-like conversion under	disorders (e.g., as described
	appropriate differentiation	below under "Neural Activity
 	conditions known in the art.	and Neurological Diseases"),
 		and infection (e.g., as
		described below under
		"Infectious Disease").

	endocrine disorders (as	described in the Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	C
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				disease dvslinidemia
				oallstones osteoarthritis
				degenerative arthritis, eating
				disorders, fibrosis, cachexia,
				and kidney diseases or
				disorders. Preferred
				indications include neoplasms
				and cancer, such as,
				lymphoma, leukemia and
				breast, colon, and kidney
				cancer. Additional preferred
				indications include melanoma,
				prostate, lung, pancreatic,
				esophageal, stomach, brain,
				liver, and urinary cancer.
				Highly preferred indications
				include lipomas and
				liposarcomas. Other preferred
				indications include benign
				dysproliferative disorders and
				pre-neoplastic conditions, such
				as, for example, hyperplasia,
				metaplasia, and/or dysplasia.
HCYBG92	1045	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and

	activation of transcription	inflammatory disorders.
	through the Nuclear Factor of	Preferred indications also
	Activated T cells (NFAT)	include blood disorders (e.g.,
	response element are well-	as described below under
	known in the art and may be	"Immune Activity", "Blood-
	used or routinely modified to	Related Disorders", and/or
	assess the ability of	"Cardiovascular Disorders").
	polypeptides of the invention	Preferred indications include
	(including antibodies and	autoimmune diseases (e.g.,
	agonists or antagonists of the	rheumatoid arthritis, systemic
	invention) to regulate NFAT	lupus erythematosis, multiple
	transcription factors and	sclerosis and/or as described
	modulate expression of genes	below) and
	involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
-	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include

				et al., Int J Biochem Cell Biol	anemia, pancytopenia,
				31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
				et al., J Immunol	leukemias, Hodgkin's disease,
				165(12):7215-7223 (2000);	acute lymphocytic anemia
				Hutchinson and McCloskey, J	(ALL), plasmacytomas,
				Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
_				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
	-			blood of a patient with mast	
**				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HDABR72	1046	Activation of	Kinase assay. Kinase assays,	A highly preferred
86			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment

		may be used or routinely	of the invention includes a
		modified to assess the ability	method for inhibiting
		of polypeptides of the	adipocyte proliferation. A
		invention (including antibodies	highly preferred embodiment
		and agonists or antagonists of	of the invention includes a
		the invention) to promote or	method for stimulating
	.,,	inhibit cell proliferation,	adipocyte differentiation. An
		activation, and differentiation.	alternative highly preferred
	475-0	Exemplary assays for ERK	embodiment of the invention
		kinase activity that may be	includes a method for
		used or routinely modified to	inhibiting adipocyte
		test ERK kinase-induced	differentiation. A highly
	,	activity of polypeptides of the	preferred embodiment of the
	<del>4114</del>	invention (including antibodies	invention includes a method
		and agonists or antagonists of	for stimulating (e.g.,
		the invention) include the	increasing) adipocyte
		 assays disclosed in Forrer et	activation. An alternative
		al., Biol Chem 379(8-9):1101-	highly preferred embodiment
		1110 (1998); Le Marchand-	of the invention includes a
		Brustel Y, Exp Clin	method for inhibiting the
		 Endocrinol Diabetes	activation of (e.g., decreasing)
		107(2):126-132 (1999);	and/or inactivating adipocytes.
		 Kyriakis JM, Biochem Soc	Highly preferred indications
		Symp 64:29-48 (1999); Chang	include endocrine disorders
		and Karin, Nature	(e.g., as described below under
ngan siamma		410(6824):37-40 (2001); and	"Endocrine Disorders").
		Cobb MH, Prog Biophys Mol	Highly preferred indications
		Biol 71(3-4):479-500 (1999);	also include neoplastic
		the contents of each of which	diseases (e.g., lipomas,
		are herein incorporated by	liposarcomas, and/or as
		reference in its entirety.	described below under

Mouse adipocyte cells that "Hyperproliferative	may be used according to these   Disorders"). Preferred		(e.g., through the ATCC). disorders (e.g., hypertension,	ıte -		according to these assays stroke, impotence and/or as	include 3T3-L1 cells. 3T3-L1 described below under	int mouse "Immune Activity",	preadipocyte cell line that is a '"Cardiovascular Disorders",	continuous substrain of 3T3 and/or "Blood-Related		through clonal isolation and (e.g., as described below under		adipose-like conversion under   disorders (e.g., as described	appropriate differentiation below under "Neural Activity	conditions known in the art. and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal
Mouse adipc	may be used	assays are pu	(e.g., through	Exemplary n	cells that may be used	according to	include 3T3-	is an adherent mouse	preadipocyte	continuous	fibroblast ce	through clon	undergo a pr	adipose-like	appropriate	conditions k			•											
																										•				

Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the
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urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly	preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with	Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies,	muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery	disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred	indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred

					indications include melanoma,
					prostate, lung, pancreatic,
	1				esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
			•		indications include benign
			•••		dysproliferative disorders and
					pre-neoplastic conditions, such
			•		as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HDHEB60	1047	Activation of	Assays for the activation of	A highly preferred indication
66			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
			•	polypeptides of the invention	An additional highly preferred
		-		(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
	****			that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve

 adipogenesis, and is involved (e.g., due to diabetic	in differentiation into   neuropathy), blood vessel	adipocytes. CRE contains the blockage, heart disease, stroke,	binding sequence for the impotence (e.g., due to diabetic	transcription factor CREB neuropathy or blood vessel	(CRE binding protein).   blockage), seizures, mental	Exemplary assays for confusion, drowsiness,	transcription through the nonketotic hyperglycemic-	cAMP response element that hyperosmolar coma,	may be used or routinely cardiovascular disease (e.g.,	modified to test cAMP- heart disease, atherosclerosis,	response element activity of microvascular disease,	polypeptides of the invention hypertension, stroke, and other	(including antibodies and diseases and disorders as	agonists or antagonists of the described in the	invention) include assays   "Cardiovascular Disorders"	disclosed in Berger et al., Gene section below), dyslipidemia,	66:1-10 (1998); Cullen and endocrine disorders (as	Malm, Methods in Enzymol described in the "Endocrine	 et al., Proc Natl Acad Sci USA   neuropathy, vision impairment	); Reusch	et al., Mol Cell Biol blindness), ulcers and impaired	20(3):1008-1020 (2000); and   wound healing, and infection	Klemm et al., J Biol Chem (e.g., infectious diseases and	273:917-923 (1998), the disorders as described in the	contents of each of which are "Infectious Diseases" section	herein incorporated by below, especially of the	reference in its entirety. Pre- urinary tract and skin), carpal	2

Dupuytren's contracture). Additional highly preferred indications are complications associated with insulin resistance.		Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and rhabdosarcoma), cardiovascular disorders (such as congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, vascular disease, and also as described below under
according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used	according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used or routinely modified to test activity of polypeptides and
		Myoblast cell proliferation
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"Cardiovascular Disorders"),	stimulating myoblast	proliferation, and innibiting	myoblast proliferation.											-		-														
antibodies of the invention	(including agonists or	antagonists of the invention)	include, for example, assays	disclosed in: Soeta, C., et al.	"Possible role for the c-ski	gene in the proliferation of	myogenic cells in regenerating	skeletal muscles of rats" Dev	Growth Differ Apr;43(2):155-	64 (2001); Ewton DZ, et al.,	"IGF binding proteins-4, -5	and -6 may play specialized	roles during L6 myoblast	proliferation and	differentiation" J Endocrinol	Mar;144(3):539-53 (1995);	and, Pampusch MS, et	al., "Effect of transforming	growth factor beta on	proliferation of L6 and	embryonic porcine myogenic	cells" J Cell Physiol	Jun;143(3):524-8 (1990); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary myoblast cells that	may be used according to these	assays include the rat myoblast	L6 cell line. Rat myoblast L6
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				cells are an adherent rat	
<del></del>				myoblast cell line, isolated	
				from animony confirmed of not	
				from primary cultures of rat	
				thigh muscle, that fuse to form	
			-	multinucleated myotubes and	
				striated fibers after culture in	
				differentiation media.	
	HDHEB60	1047	Production of	Assays for measuring	Highly preferred indications
66			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
				agonists or antagonists of the	inflammatory disorders,
				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
_				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
				vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
_				not limited to, angiogenesis,	Disorders"). Highly preferred
_				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
		_		endothelial cells that may be	melanoma, renal cell
_				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,

cell-mediated immune response. Additional highly preferred indications include inflammation and	additional highly preferred indication is infection (e.g., an infectious disease as described	below under "Infectious Disease"). Preferred indications include neoplastic	lymphoma, and/or as described below under	"Hyperproliferative Disorders"). Preferred	indications include neoplasms and cancers, such as, for	example, leukemia, lymphoma, and prostate, breast, lung,	colon, pancreatic, esophageal, stomach, brain, liver and	urinary cancer. Other preferred indications include benign	dysproliferative disorders and nre-neonlastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	include anemia, pancytopenia,	leukopenia, thrombocytopenia,
transcription through the NFAT response element that may be used or routinely modified to test NFAT-	response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Aramburu et al., J Exp Med	182(3):801-810 (1995); De Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol	29(3):838-844 (1999); and Yeseen et al., J Biol Chem	268(19):14285-14293 (1993), the contents of each of which	are herein incorporated by reference in its entirety. NK	cells that may be used	according to these assays are	through the ATCC).	Exemplary human NK cells

Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as
that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that
	Activation of transcription through NFKB response element in immune cells (such as natural killer cells).
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described below). An additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute
may be used or rountinely modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	NK cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary NK cells that may	be used according to these	assays include the NK-YT cell	line, which is a human natural	killer cell line with cytolytic	and cytotoxic activity.
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lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described
	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions.  Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element
	Activation of transcription through AP1 response element in immune cells (such as T-cells).
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-		the invention) include assays   immunodeficiencies (e.g., as	disclosed in Berger et al., Gene described below). Additional	66:1-10 (1988); Cullen and highly preferred indications	Malm, Methods in Enzymol   include inflammation and	216:362-368 (1992); Henthorn   inflammatory disorders.	et al., Proc Natl Acad Sci USA   Highly preferred indications		Rellahan et al., J Biol Chem diseases (e.g., leukemia,	···	Chang et al., Mol Cell Biol below under	18(9):4986-4993 (1998); and "Hyperproliferative	Fraser et al., Eur J Immunol Disorders"). Highly preferred	29(3):838-844 (1999), the indications include neoplasms	contents of each of which are and cancers, such as, leukemia,	herein incorporated by lymphoma, prostate, breast,	reference in its entirety.   lung, colon, pancreatic,		used according to these assays liver, and urinary cancer. Other	are publicly available (e.g., preferred indications include	through the ATCC). benign dysproliferative	Exemplary human T cells that disorders and pre-neoplastic	may be used according to these   conditions, such as, for	assays include the SUPT cell example, hyperplasia,	line, which is an IL-2 and IL-4   metaplasia, and/or dysplasia.		oell line arthritis asthma AIDS.			
Cotton and other	and agonists or antag	the invention) includ	disclosed in Berger e	66:1-10 (1988); Cull	Malm, Methods in E	216:362-368 (1992);	et al., Proc Natl Acad	85:6342-6346 (1988)	Rellahan et al., J Bio	272(49):30806-3081	Chang et al., Mol Ce	18(9):4986-4993 (19	Fraser et al., Eur J In	29(3):838-844 (1999	contents of each of w	herein incorporated l	reference in its entire	Human T cells that r.	used according to the	are publicly availabl	through the ATCC).	Exemplary human T	may be used accordi	assays include the Sl	line, which is an IL-	responsive suspension	aul line	CCII IIIIC:		
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plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for includes a method for stimulating (e.g., increasing) IL-2 production. An alternative
	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and
	Activation of transcription through CD28 response element in immune cells (such as T-cells).
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Company of the Compan			Malm, Methods in Enzymol	highly preferred embodiment
			216:362-368 (1992); Henthorn	of the invention includes a
			et al., Proc Natl Acad Sci USA	method for inhibiting (e.g.,
			85:6342-6346 (1988);	reducing) IL-2 production.
			McGuire and Iacobelli, J	Additional highly preferred
			Immunol 159(3):1319-1327	indications include
			(1997); Parra et al., J Immunol	inflammation and
		i.	166(4):2437-2443 (2001); and	inflammatory disorders.
			Butscher et al., J Biol Chem	Highly preferred indications
			3(1):552-560 (1998), the	include autoimmune diseases
			contents of each of which are	(e.g., rheumatoid arthritis,
			herein incorporated by	systemic lupus erythematosis,
			reference in its entirety. T	multiple sclerosis and/or as
			cells that may be used	described below),
	-		according to these assays are	immunodeficiencies (e.g., as
			publicly available (e.g.,	described below), boosting a T
			through the ATCC).	cell-mediated immune
			Exemplary human T cells that	response, and suppressing a T
			may be used according to these	cell-mediated immune
			assays include the SUPT cell	response. Highly preferred
			line, which is a suspension	indications include neoplastic
	.,,.		culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
			responsive T cells.	cell carcinoma, leukemia,
				lymphoma, and/or as described
				below under
				"Hyperproliferative
				Disorders"). Highly preferred
				indications include neoplasms
				and cancers, such as, for
	_			example, melanoma (e.g.,
				metastatic melanoma), renal

cell carcinoma (e.g., metastatic renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma), and prostate,	breast, lung, colon, pancreauc,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	A highly preferred indication	includes infection (e.g.,	AIDS, tuberculosis, infections	associated with granulomatous	disease, and osteoporosis,	and/or as described below	under "Infectious Disease"). A	highly preferred indication is	AIDS. Additional highly	preferred indications include	suppression of immune	reactions to transplanted	organs and/or tissues, uveitis,	psoriasis, and tropical spastic	paraparesis. Preferred	indications include blood	disorders (e.g., as described	below under "Immune
					13-1																							
		•														<del>Maria de</del>											-	
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Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").  Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allerov	S P
	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression
	Activation of transcription through GAS response element in immune cells (such as T-cells).
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melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral
involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).		
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				-									-																	

				infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is
				Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and
нрнев60	1047	Activation of transcription through NFAT response element in	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-

immune cells (such are well-known in the art and readiovaried by the continuity of polypeptides of the invention (including antibodies) and agonists or antagonists of polypeptides of the invention (including antibodies) (e.g., rheumatoid arthritis, and agonists or antagonists or antagonist of immunatoid arthritis, and agonists or prepared including antibodies (e.g., rheumatoid arthritis, and agonists or prepared including antibodies (e.g., rheumatoid arthritis) and agonists or antagonists of the invention include assays for response element activity of inflammation and including antibodies and indication include assays in the continuity of including antibodies and indication include assays of the invention and indication is infectious diseases as described (66:1-10 (1998); Cullen and indications include neoplastic et al., Proc Natl Acad Sci USA (1989); Henthom and care ano
immune cells (such as T-cells).

			100,000	Fraser et al Eur J Immunol	and prostate, breast, lung,
				29(3):838-844 (1999); and	colon, pancreatic, esophageal,
				Yeseen et al. J. Biol Chem	stomach, brain, liver and
				268(19):14285-14293 (1993).	urinary cancer. Other preferred
				the contents of each of which	indications include benign
				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. T	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
	1-2-2			publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human T cells that	leukopenia, thrombocytopenia,
		-		may be used according to these	Hodgkin's disease, acute
				assays include the SUPT cell	lymphocytic anemia (ALL),
				line, which is a suspension	plasmacytomas, multiple
				culture of IL-2 and IL-4	myeloma, Burkitt's lymphoma,
				responsive T cells.	arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
		•			reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
				and the state of t	asthma and allergy.
	HDHEB60	1047	Activation of	Assays for the activation of	Highly preferred indications
66			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
		.,	response element in	well-known in the art and may	Highly preferred indications
				A substitute of the substitute	

		immune cells (such	be used or routinely modified	include blood disorders (e.g.,
-		as T-cells).	to assess the ability of	as described below under
		`	polypeptides of the invention	"Immune Activity", "Blood-
			including antibodies and	Related Disorders", and/or
			agonists or antagonists of the	"Cardiovascular Disorders").
			invention) to regulate NFKB	Highly preferred indications
			transcription factors and	include autoimmune diseases
			modulate expression of	(e.g., rheumatoid arthritis,
			immunomodulatory genes.	systemic lupus erythematosis,
			Exemplary assays for	multiple sclerosis and/or as
			transcription through the	described below), and
			NFKB response element that	immunodeficiencies (e.g., as
			may be used or rountinely	described below). An
	-		modified to test NFKB-	additional highly preferred
			response element activity of	indication is infection (e.g.,
0.9			polypeptides of the invention	AIDS, and/or an infectious
 84			including antibodies and	disease as described below
_			agonists or antagonists of the	under "Infectious Disease").
			invention) include assays	Highly preferred indications
			disclosed in Berger et al., Gene	include neoplastic diseases
			66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
			Malm, Methods in Enzymol	lymphoma, and/or as described
			216:362-368 (1992); Henthorn	below under
			et al., Proc Natl Acad Sci USA	"Hyperproliferative
			85:6342-6346 (1988); Black et	Disorders"). Highly preferred
			al., Virus Gnes 15(2):105-117	indications include neoplasms
			(1997); and Fraser et al.,	and cancers, such
			29(3):838-844 (1999), the	as,melanoma, renal cell
-			contents of each of which are	carcinoma, leukemia,
			herein incorporated by	lymphoma, and prostate,
			reference in its entirety. T	breast, lung, colon, pancreatic,

			cells that may be used	esophageal, stomach, brain,
			according to these assays are	liver and urinary cancer. Other
			publicly available (e.g.,	preferred indications include
			through the ATCC).	benign dysproliferative
			Exemplary human T cells that	disorders and pre-neoplastic
			may be used according to these	conditions, such as, for
			assays include the SUPT cell	example, hyperplasia,
-		-	line, which is a suspension	metaplasia, and/or dysplasia.
			culture of IL-2 and IL-4	Preferred indications also
			responsive T cells.	include anemia, pancytopenia,
د				leukopenia, thrombocytopenia,
_	•			Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS,
	***			granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				suppression of immune
				reactions to transplanted
,				organs, asthma and allergy.
HDHEB60	1047	Activation of	Assays for the activation of	A highly preferred
		transcription	transcription through the	indication is allergy.
		through STAT6	Signal Transducers and	Another highly preferred
		response element in	Activators of Transcription	indication is asthma.
		immune cells (such	(STAT6) response element are	Additional highly preferred

indications include inflammation and inflammatory disorders.	blood disorders (e.g., as described below under "Immune Activity", "Blood-	Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below).	Preferred indications include neoplastic diseases (e.g.,	leukemia, lymphoma, melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Preferred indications include neoplasms	and cancers, such as, leukemia, lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver and	urinary cancer. Other preferred
well-known in the art and may be used or routinely modified to assess the ability of	(including antibodies and agonists or antagonists of the invention) to regulate STAT6	transcription factors and modulate the expression of multiple genes. Exemplary	assays for transcription through the STAT6 response	element that may be used or routinely modified to test	activity of the polypeptides of the invention (including	antibodies and agonists or antagonists of the invention)	include assays disclosed in Berger et al., Gene 66:1-10	(1998); Cullen and Malm, Methods in Enzymol 216:362-	368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538	(1998); Moffatt et al.,	Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur	J Immunol 27(8):1982-1987
as T-cells).											J 11		
										,			

				(1997); and Masuda et al J	indications include benian
				Biol Chem 275(38):29331-	dysproliferative disorders and
		<del></del>		29337 (2000), the contents of	pre-neoplastic conditions, such
				each of which are herein	as, for example, hyperplasia,
				incorporated by reference in its	metaplasia, and/or dysplasia.
				entirety. T cells that may be	Preferred indications include
				used according to these assays	anemia, pancytopenia,
				are publicly available (e.g.,	leukopenia, thrombocytopenia,
				through the ATCC).	Hodgkin's disease, acute
				Exemplary T cells that may be	lymphocytic anemia (ALL),
				used according to these assays	plasmacytomas, multiple
			774	include the SUPT cell line,	myeloma, Burkitt's lymphoma,
<del></del>				which is a suspension culture	arthritis, AIDS, granulomatous
	89-ya			of IL-2 and IL-4 responsive T	disease, inflammatory bowel
			-	cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
		-2-			diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additional preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
	100				Disease").
	HDHIA94	1048	Production of TNF	TNFa FMAT. Assays for	A highly preferred
100			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
		-	cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)

	fibroblasts smooth muscle	TNF alnha production An	_
-	 and other soll times that are a		
	and other cen types that exert a	alternative highly preferred	
	wide variety of inflammatory	embodiment of the invention	
	and cytotoxic effects on a	includes a method for	
-	variety of cells are well known	stimulating (e.g., increasing)	
	 in the art and may be used or	TNF alpha production.	
	routinely modified to assess	Highly preferred indications	_
	the ability of polypeptides of	include blood disorders (e.g.,	
	the invention (including	as described below under	
	antibodies and agonists or	"Immune Activity", "Blood-	
	antagonists of the invention) to	Related Disorders", and/or	
	mediate immunomodulation,	"Cardiovascular Disorders"),	
	modulate inflammation and	Highly preferred indications	
	cytotoxicity. Exemplary	include autoimmune diseases	
	assays that test for	(e.g., rheumatoid arthritis,	
	immunomodulatory proteins	systemic lupus erythematosis,	
	evaluate the production of	Crohn"s disease, multiple	
	 cytokines such as tumor	sclerosis and/or as described	
	necrosis factor alpha (TNFa),	below), immunodeficiencies	
	and the induction or inhibition	(e.g., as described below),	
	of an inflammatory or	boosting a T cell-mediated	
	cytotoxic response. Such	immune response, and	
	assays that may be used or	suppressing a T cell-mediated	
	routinely modified to test	immune response. Additional	
	immunomodulatory activity of	highly preferred indications	
	polypeptides of the invention	include inflammation and	
	(including antibodies and	inflammatory disorders, and	
	agonists or antagonists of the	treating joint damage in	
	invention) include assays	patients with rheumatoid	
	disclosed in Miraglia et al., J	arthritis. An additional highly	
	Biomolecular Screening 4:193-	preferred indication is sepsis.	

Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,
204(1999); Rowland et al.,	connected Placifical	approach Chapter 0:138-100 (2000): Verhasselt et al Eur I	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.					
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neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Theotious Disease.")	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred
	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB.
	Activation of transcription through NFKB response element in immune cells (such as natural killer cells).
	1049
	HDHMA72
	101

indication is infection (e.g., AIDS, and/or an infectious disease as described below	under "Infectious Disease"). Highly preferred indications		(e.g., melanoma, leukemia, lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas multiple
response element activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	NK cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NKL	cell line, which is a human	natural killer cell line	established from the peripheral	blood of a patient with large	granular lymphocytic

				leukemia. This IL-2 dependent suspension culture cell line has a morphology resembling that of activated NK cells.	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.
102	HDLAC10	1050	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lums erythematosis

	antagonists of the invention)	Crohn"s disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
****	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
	dependent suspension culture	highly preferred indications
	of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
		leukemia, lymphoma,
 		melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other

				17.71	preferred indications include
		-			benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
		1-4			reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
,					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HDLAC10	1050	Production of	Assays for measuring	Highly preferred indications
			VCAM in	expression of VCAM are well-	include inflammation (acute

	endothelial cells	known in the art and may be	and chronic). restnosis.
-	(such as human	used or routinely modified to	atherosclerosis, asthma and
	umbilical vein	assess the ability of	allergy. Highly preferred
	endothelial cells	polypeptides of the invention	indications include
	(HUVEC))	(including antibodies and	inflammation and
		agonists or antagonists of the	inflammatory disorders,
		invention) to regulate VCAM	immunological disorders,
		expression. For example,	neoplastic disorders (e.g.
		FMAT may be used to meaure	cancer/tumorigenesis), and
		the upregulation of cell surface	cardiovascular disorders (such
		VCAM-1 expresssion in	as described below under
		endothelial cells. Endothelial	"Immune Activity", "Blood-
		cells are cells that line blood	Related Disorders",
		vessels, and are involved in	"Hyperproliferative Disorders"
		functions that include, but are	and/or "Cardiovascular
		not limited to, angiogenesis,	Disorders"). Highly preferred
		vascular permeability, vascular	indications include neoplasms
•		tone, and immune cell	and cancers such as, for
		extravasation. Exemplary	example, leukemia, lymphoma,
		endothelial cells that may be	melanoma, renal cell
		used according to these assays	carcinoma, and prostate,
		include human umbilical vein	breast, lung, colon, pancreatic,
		endothelial cells (HUVEC),	esophageal, stomach, brain,
		which are available from	liver and urinary cancer. Other
-		commercial sources. The	preferred indications include
		expression of VCAM	benign dysproliferative
		(CD106), a membrane-	disorders and pre-neoplastic
		associated protein, can be	conditions, such as, for
	,	upregulated by cytokines or	example, hyperplasia,
		other factors, and contributes	metaplasia, and/or dysplasia.
		to the extravasation of	

		highly preferred embodiment of the invention includes a
lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the	assays discressed in Folier et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-
	Activation of Adipocyte ERK Signaling Pathway	
	1052	
	HDPBI32	
	104	

method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications		(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under
Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.		
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				-																						7.416				

section below), dyslipidemia,	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,
		-				-												-											

hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign diposarcomas. Other preferred indications include benign dysproliferative disorders and dysproliferative disorders and dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia.	Highly preferred indications include eosinophilia, asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune
	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of increases in the ability of polypeptides of increases increases in the ability of polypeptides of increases increases increases in the ability of polypeptides of increases incr
	Regulation of viability or proliferation of immune cells (such as human eosinophil EOL-1 cells).
	1053
	НДРВQ71
1000	105